THE CHEMISTRY OF ADDUCTS

FROM ACETYLENES AND QUINALDINES

A Thesis presented

by

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in part fulfilment

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EXPLANATORY NOTE

The letter E denotes the group -CO$_2$Me in structural formulae throughout.

The u.v., n.m.r. and mass spectral data for all compounds in Part One are presented in Tables 9, 10 and 11 respectively. For convenience, certain spectral data are repeated in subsidiary tables at appropriate points in the main text. The spectral data for the blue adducts are given in Part Two.

N.m.r. spectra are reported as $\tau$-values, with coupling constants (J) in Hz; d = doublet, m = multiplet. Ultraviolet absorption maxima are quoted in nm, with $10^{-4}\epsilon$ in parentheses; br = broad, infl. = point of inflexion.

Compound numbers in the Experimental Section are the same as those in the text.
PART ONE

Chapter 1

The Reactions of Acetylenecarboxylic Acids and Their Esters with Nitrogen-Containing Heterocyclic Compounds
Acetylenic acids and their esters react with nitrogen-containing heterocycles to give adducts which display a wide variety of structures. A detailed review was published in 1953; more recent work has also been reviewed

It is generally possible to account for the formation of such adducts by assuming an initial Michael-type addition to give a zwitterion such as (1) or (2)

\[ \text{addition to give a zwitterion such as (1) or (2)} \]

This initial zwitterion may then react further in a number of ways.

(a) It may undergo an intramolecular proton-shift or gain a proton from solvent or other reactant. Thus zwitterion (2), from 1-benzylpyrrole and acetylenedicarboxylic acid, rearranges to give a mixture of the fumaric and maleic acids (3). Dimethyl acetylenedicarboxylate reacts similarly with
pyrroles, pyrazoles, imidazoles, indazoles and indoles, the products being mixtures of the corresponding maleate and fumarate esters.

Acridine with dimethyl acetylenedicarboxylate in methanol gives the methoxide which is in equilibrium with the 9-methoxy-9,10-dihydroacridine; the zwitterion presumably abstracts a proton from the solvent methanol. 2,3-Benzacridine, phenanthridine and phthalazine in methanol react similarly; and pyridine and isoquinoline give analogous products with methyl propiolate in methanol.

(b) The initial zwitterion may cyclise directly. Indolizine with dimethyl acetylenedicarboxylate in the presence of palladium charcoal gives the cycl[3,2,2]azine derivatives, possibly by the following mechanism. Woodward and Hoffmann however have pointed out that this reaction may be described as an [8+2] cyclo-addition reaction.
Diels-Alder adducts are also obtained in a few cases. Indeed, the reactions of acetylenes with heterocycles were first investigated by Diels and Alder shortly after their discovery of the reaction which now bears their names; their attention was drawn to potential diene systems such as furan\textsuperscript{23-24} and pyrrole\textsuperscript{25}.

The adduct(9) is a minor product of the reaction of 1-benzylpyrrole with acetylenedicarboxylic acid; it is very likely that reaction proceeds via the intermediate(2), and thus the term "Diels-Alder" is perhaps better used to describe the product of reaction rather than the reaction mechanism.

\[ \text{1-Methylpyrrole with dimethyl acetylenedicarboxylate gives the dihydroindole derivative}(11)\textsuperscript{5,26}. \] This is readily explained by a two-step reaction; the initially-formed Diels-Alder adduct(10), which was not isolated, adds a
second mole of the ester to give the product (11) as shown.

An analogous case in the isoindole series has recently been reported; here the Diels-Alder adduct (12) was isolated and shown to react further with the ester to give the dihydroindole derivative (13), analogous to (11).

Further recent examples of Diels-Alder adducts occur in the pyrimidine and pyrazine series.

(c) The initial zwitterion may attack another electrophile that may be present in the reaction mixture. Pyridine, some alkylpyridines and isoquinoline react with dimethyl acetylenedicarboxylate and carbon dioxide at -60° to give unstable adducts such as (14).

(d) The initial zwitterion may attack a second mole of acetylenic ester and then cyclise. Many pyridines react
with dimethyl acetylenedicarboxylate under aprotic conditions to give 9aH-quinolizines (15), some of which may readily be isomerised to the 4H-quinolizines (16). Analogous reactions occur with quinoline, imidazoles

![Chemical Reaction](image)

Analogous reactions occur with quinoline, imidazoles and many other heterocycles with pyridine-type nitrogen atoms. Related compounds such as 2-methylquinoline (quinaldine) also give quinolizines, but the presence of active methyl groups frequently leads to more complicated reactions, discussed below (p. 7).

A minor product of the reaction of phenanthridine with dimethyl acetylenedicarboxylate is the oxazine (18); here the initial zwitterion (17) attacks a second mole of ester in the alternate manner shown.

![Chemical Structures](image)
Scheme 1.

\[
\text{Scheme 1.}
\]

(1) \[ \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \]

(19) \[ \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \]

(20) \[ \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \]

(21) \[ \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \rightarrow \text{EE} \]
(e) The initial zwitterion may add solvent, then a second mole of acetylenic ester and cyclise. Thus pyridine with dimethyl acetylenedicarboxylate in methanol (Scheme 1) gives a mixture of products (20) and (21); it is assumed that the species(19) undergoes a Michael addition of methoxide anion under the influence of both the positive charge on the ring and the assisting ester group.

(f) More recent work has indicated that the initial zwitterion may react in yet further ways. 2,4-Dimethylthiazole with two moles of dimethyl acetylenedicarboxylate gives the azepine(25); similar reactions occur with 2-alkylthiazolines, 3,6-dimethylpyridazine, 1,2-disubstituted benzimidazoles, 2-alkylbenzoxazoles, 2-alkylbenzothiazoles, 2-methylbenzoselenazole and 2-methylquinoline. The formation of these azepines may be explained by assuming that the initial zwitterion(22)
undergoes proton transfer from the activated methyl group to give the new zwitterion (23), which then adds a second mole of ester and cyclises as shown.

A minor product of the reaction with 2-benzyl-1-methylbenzimidazole is the compound (27), formation of which is readily explained by assuming that the intermediate (26), analogous to (24), cyclises in the following alternate manner.

A major product of the reaction of 2-methylquinoline with dimethyl acetylenedicarboxylate in ether or acetonitrile is the azepine (28), formation of which appears at first sight to involve the migration of an ester group.

Analogous reactions have been observed with 1-methylisoquinoline, 6-methylphenanthridine, 4-methylpyrimidines, 4-methylquinazoline, 2-methylquinoxalines and 2-methylbenzoxazole. Isomeric azepines such as (29) are obtained in a few cases (cf. p. 13). The formation of these azepines is discussed in detail in Chapter 2.
Scheme 2.

\[ \text{Scheme 2.} \]

\[ \text{(33)} \]

\[ (34) \quad R = \text{Me} \]

\[ (35) \quad R = \text{Et} \]

\[ (36) \]

\[ (37) \quad R = \text{Me} \]

\[ (38) \quad R = \text{Et} \]
The occurrence of ester-shifts is more widespread than has perhaps hitherto been appreciated; the subject has been reviewed recently. A example is the rearrangement of the 1-methylpyrrole adduct (30) to the isomer (32) on heating to ca. 200\degree with palladised charcoal. The proposed mechanism involves nucleophilic attack, promoted by the nitrogen lone-pair electrons, of the 3-position at the 3a-carbonyl group to give the intermediate (31). This intermediate is similar to the cyclopropanone intermediate suggested for the Favorskii rearrangement of \(\alpha\)-haloketones.

In contrast to active-methyl compounds such as 2-methylquinoline, 1-methylisoquinoline and others mentioned above, 2-methylpyridine does not form adducts involving the active methyl group. However methyl 2-pyridylacetate, which possesses a more acidic 2-methylene group, reacts with dimethyl and diethyl acetylene-dicarboxylate in ether to give respectively the 2-quinolizones (34) and (35) and the 4-quinolizones (37) and (38) (Scheme 2). The loss of the pyridine ester group in the formation of (35) indicates (path A) that reaction proceeds via an initial zwitterion (33) in the usual way. However
the retention of this group in the formation of (37) and (38) suggests that nucleophilic attack on the acetylene can also occur from the activated methylene group via an intermediate (36) (path B). Winterfeldt has investigated the reaction of methyl 2-pyridylacetate with dimethyl acetylenedicarboxylate in t-butanol and has obtained complementary results. Other examples in the pyridine series of attack initiated from activated 2-substituents have also been reported.\(^{51,52}\)

The quinoline (39) is the sole product of the reaction of 8-bromo-2-methylquinoline with dimethyl acetylenedicarboxylate.\(^{45}\)

\[ \text{quinoline (39)} \]

\[ \text{Br} \]

\[ \text{E} \]

\[ \text{H} \]

\[ \text{H} \]

\[ \text{H} \]

Analogues have now been obtained from several 8-substituted 2-methylquinolines (p. 58). Presumably the steric effect of the 8-substituent alters the position of greatest nucleophilic reactivity from the nitrogen atom to the methyl group; and after initial attack by the species (40), analogous to (36), a prototropic shift occurs to bring the side-chain double bond into conjugation with the ring. Carbanions such as (36) and (40) now appear to be of great importance in the reactions of acetylenes with heterocycles containing active methyl and methylene groups; the question is discussed fully in Chapter 2.
Various heterocyclic N-oxides react with acetylenic esters to give ylides of type (41). The reaction has been successfully applied to N-oxides of phenanthridines, benzimidazoles, isoquinoline and 5,4-dihydroisoquinoline. Formation of these ylides requires migration of an oxygen atom; various mechanisms have been proposed. Certain 6-substituted 5-oxidovinyl phenanthridiniums (41) exhibit both cis-trans and rotational isomerism; the effect has recently been studied using variable-temperature n.m.r. spectroscopy.

Indoles have recently been shown to behave as enamines in certain reactions with acetylenic esters. The azepine (43) is a product of the reaction of 1-methylindole with dimethyl acetylenedicarboxylate, and the following mechanism for its formation has been proposed.

Cyclobutenes analogous to (42) have been isolated from
the reactions of enamines with unsaturated esters,\textsuperscript{59-61} and of some 1,4-dihydropyridines with dimethylacetylene-dicarboxylate.\textsuperscript{62} Liu and Snieckus have also obtained the azepines (44) and (45) from the reactions of 1-acetyl-3-piperidinoindole with dimethyl acetylene dicarboxylate and methyl propiolate; the intermediate cyclobutene (46) was isolated and shown to undergo rearrangement to (45).

\[\text{CO Me.} \]

(44) \hspace{1cm} (45) \hspace{1cm} (46)

Acetylenes may react with heterocycles in other ways. Huisgen has proposed a concerted 1,4-dipolar cycloaddition mechanism for some reactions of dimethyl acetylene dicarboxylate;\textsuperscript{64} however this mechanism has not been rigorously established.

Acetylenic esters themselves polymerize readily, and ester polymers are frequently isolated from reaction mixtures. A tetramer of dimethyl acetylene dicarboxylate has been assigned the structure (47);\textsuperscript{65-67} the carbene

\[\text{OMe} \]

(47) \hspace{1cm} (48)
form (48) of the ester has been invoked to account for the formation of this compound.

The adducts discussed so far are formed by reaction of one mole of the heterocycle with at most two moles of the acetylene. Some adducts formed from more than two moles of the acetylene have been characterised; for example, cycl[3,2,2]azines such as (49) from pyridines and methyl propiolate, and the adduct (50) from 2,4-dimethylquinazoline and dimethyl acetylenedicarboxylate.

![Image](49)

![Image](50)

The reaction of 2-methylquinoline with dimethyl acetylene dicarboxylate in ether or acetonitrile solution is reported to give the benzo[c]quinolizine (51), the azepine (28) already mentioned, and, in low yield, "red" and "blue" adducts which are formed from more than two moles of the ester. Isolation of an "apple-green" adduct

![Image](51)

![Image](28)
has also been reported on one occasion; a colourless aduct reported by Diels and Kech has not been found by subsequent workers. "Red" and "blue" aducts have also been isolated from the reaction of 2,8-dimethyl-quinoline with dimethyl acetylenedicarboxylate in benzene.

Analysis and mass spectra show that the red aducts are formed from one mole of the quinoline and three moles of the ester. Gagan obtained n.m.r., i.r. and u.v. spectral data for these aducts and also isolated hydrogenation products, and made tentative suggestions regarding structure. Caterer, using Gagan's data along with the mass spectra, assigned structures but offered no chemical evidence for these. Both workers considered that these aducts were analogues, the only difference between them being the presence of the extra methyl group in the benzo-ring of the 2,8-dimethylquinoline aduct.

Gagan reported the isolation of only one red aduct from the reactions of both 2-methyl- and 2,8-dimethyl-quinoline with the ester; however Caterer appears to have known of the formation of two red aducts from 2-methylquinoline. Caterer also showed by thin-layer chromatography that two red aducts and a blue aduct are formed in the reactions of 2,6-dimethylquinoline with both dimethyl and diethyl acetylenedicarboxylate.

Gagan and Caterer also made suggestions as to the structures of the blue aducts, but again they offered no chemical evidence in support of these.
The immediate object of the present research has been to elucidate the structures of these "red" and "blue" adducts, using chemical and physical methods. The reactions of a number of substituted 2-methylquinolines with dimethyl acetylenedicarboxylate have been investigated with a view to preparing further red and blue adducts. It was also hoped to study what effects, if any, the introduction of further substituents into the quinoline ring would have on the formation of these red and blue adducts.

The red adducts have been investigated using chemical and spectroscopic methods and are discussed in Part One of this thesis. During the course of this work several new benzo[c]quinolizines and azepines (Chapter 2) and other adducts (Chapter 4) have been isolated. The blue adducts have been investigated by means of X-ray crystallography and are discussed in Part Two.
Chapter 2

New Azepines from Substituted 2-Methylquinolines and Acetylenedicarboxylates
2-Methylquinoline reacts with dimethyl acetylenedicarboxylate in acetonitrile or ether solution to give tetramethyl 4a-methyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (51), tetramethyl 10,11-dihydroazepino[1,2-a]quinoline-7,8,9,10-tetracarboxylate (28) and small amounts of "dark red" and "blue" adducts. The benzo[c]quinolizines and azepines isolated from the reactions of certain substituted 2-methylquinolines with dimethyl acetylenedicarboxylate are discussed in this chapter.

Acetonitrile appears to be the best solvent for these reactions, a reflection of the polar nature of the products and the intermediates involved in their formation. When the 8-position of the 2-methylquinoline is unsubstituted, reaction proceeds rapidly at room temperature. Reactions with 8-substituted 2-methylquinolines require heating or longer reaction times (perhaps several weeks at room temperature); this is presumably a consequence of steric
hindrance to attack at the nitrogen atom.

2,3-Dimethylquinoline with dimethyl acetylene-dicarboxylate gave the benzo[c]quinolizine (52), the azepines (58) and (64), and, in low yield, a dark green adduct (p. 27).

\[
\begin{align*}
(52) & \quad 5-\text{Me} \\
(53) & \quad 6-\text{Me} \\
(54) & \quad 10-\text{Me} \\
(55) & \quad 6-\text{Cl} \\
(56) & \quad 5-\text{Ph} \\
(57) & \quad 6,8,10-\text{Me}_3 \\
(58) & \quad 6-\text{Me} \\
(59) & \quad 5-\text{Me} \\
(60) & \quad 1-\text{Me} \\
(61) & \quad 5-\text{Cl} \\
(62) & \quad 6-\text{Ph} \\
(63) & \quad 5-\text{OMe} \\
(64) & \quad 6-\text{Me} \\
(29) & \quad 3-\text{Br}
\end{align*}
\]

The benzo[c]quinolizine (53), not detected in the previous study, was obtained in addition to the azepine (59) from dimethyl acetylenedicarboxylate and 2,4-dimethylquinoline. 2,8-Dimethylquinoline with the ester gave the benzo[c]quinolizine (54) and the azepine (60), as well as red and blue adducts (Chapter 3) and three further adducts (Chapter 4). Only the red and blue adducts were reported previously.

The benzo[c]quinolizine (55) and the azepine (61) were isolated from the reaction with 4-chloro-2-methylquinoline.
Table 1
Spectral Data for Selected Benz[g]quinolizines and Azepines

<table>
<thead>
<tr>
<th>Compound</th>
<th>N.M.R. Spectra</th>
<th>U.V.Spectra (in methanol): $\lambda_{\text{max}}$ (nm) ($10^{-4} \varepsilon$)</th>
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<tr>
<td>(52) ArH(4), 6-Me</td>
<td>2.67-3.05 m; 4a-Me, 8.56; 5-Me, 7.88; 6-H, 3.67; ester-Me, 6.18, 6.24, 6.33, 6.51</td>
<td>255 (2.04), 295 (0.61), 386 (0.47)</td>
</tr>
<tr>
<td>(55) ArH(4), 6-Cl</td>
<td>2.33-2.43 m, 2.65-2.93 m; 4a-Me, 8.49; 5-H, 3.37; ester-Me, 6.16, 6.22, 6.31, 6.39</td>
<td>246 (1.45), 291 (0.46), 310 (0.30), 391 (0.39)</td>
</tr>
<tr>
<td>(58) ArH(4), 6-Cl</td>
<td>2.6-3.1 m; 6-Me, 7.50; 10-H, 11-H_A, ca. 6.3 m; 11-H_C, 7.5 m; ester Me, 6.18, 6.29, 6.29, 6.37</td>
<td>224 (2.12), 261 (0.73), 270 (0.87), 281 (1.02), 300 (1.07), 311 (1.16), 324 (0.83), 405 (0.67), 426 (0.90), 447 (0.85), 475 (0.47)</td>
</tr>
<tr>
<td>(61) ArH, 6-Cl</td>
<td>2.15-2.95 m; 10-H, 11-H_A, 6.2-6.57 m; 11-H_C, 7.39 m; ester-Me, 6.20, 6.28-6.34</td>
<td>223 (2.96), 271 (1.45), 278 (1.65), 299 (2.37), 311 (2.18), 323 (1.61), 418 (0.68), 438 (0.89), 462 (0.86), 493 (0.45)</td>
</tr>
</tbody>
</table>
2-Methyl-3-phenylquinoline gave the benzo[c]quinolizine (56) and the azepine (62) along with a trace of an unidentified yellow compound. The benzo[c]quinolizine (57) was obtained along with four other adducts (Chapter 4) from the reaction with 2,4,6,8-tetramethylquinoline; no azepine was isolated from this reaction.

These compounds were identified by consideration of their n.m.r. (Table 10), i.r. and u.v. (Table 9) spectra, and in the case of azepines mass spectral data (Table 11), and are entirely analogous to benzo[c]quinolizines and azepines already obtained from other 2-methylquinolines. For convenience, u.v. and n.m.r. spectral data for selected examples are collated in Table 1. The benzo[c]quinolizines are non-basic; the u.v. spectra remain unchanged in strongly acidic solution. The azepines protonate readily; the resulting quinolinium-type chromophores indicate that protonation occurs at position 7 to give ions such as (65).  

![Image of molecule](image)

The n.m.r. spectra of the azepines (58)-(62) show the characteristic ABX patterns (partly obscured by ester-methyl and aromatic-methyl resonances) of the CH\(_2\)-CH\(\equiv\) group. The 7-ester group of the 2-methylquinoline azepine (28) deshields the 6-proton; so that in spite of
being β to the nitrogen atom this proton appears at a τ-value (2.32) below that of the 5-proton (2.74) (doublets, CDCl₃ solution). These resonances are definitely assignable by comparison with the spectra of the azepines from 2,3-dimethylquinoline (58) (5-proton obscured by multiplet, 2.6-3.1τ) and 2,4-dimethylquinoline (59) (6-proton, 2.43τ).

The n.m.r. spectrum of the azepine (62) from 2-methyl-3-phenylquinoline shows a very high-field 3-proton singlet (7.05τ) which is assigned to the 7-ester group, shielded by the peri 6-phenyl ring. A similar shielding effect was observed in the case of the 9aH-quinolizine (66), from 2-phenylpyridine and dimethyl acetylenedicarboxylate; the 4-ester group, shielded by the peri 6-phenyl group, appears at 7.0τ.

![Diagram](66)

The 11-ester group of the azepine (64) from 2,3-dimethylquinoline is shielded similarly by the benzo-ring, but to a lesser degree. Here also the 1-proton is moved upfield as it is present in the shielded area above or below the 11-ester carbonyl group. The spectrum of the azepine (29) from 6-bromo-2-methylquinoline shows
similar shielding effects.

The methoxy-azepine(63) was obtained by heating the chloro-azepine(61) with methanolic hydrogen chloride under reflux. Compound(63) could be formed by hydrolysis to the enol followed by methylation, or possibly by direct nucleophilic displacement of chloride ion. Attempts to prepare the 5-hydroxyazepine or a keto-tautomer by hydrolysis with aqueous-methanolic hydrochloric acid gave a mixture; the n.m.r. spectrum of the product shows a very complex ester region, indicating partial hydrolysis of the ester groups. The spectrum also indicates however that hydrolysis and tautomerisation to a keto-form does occur; a broad, downfield doublet at 1.67 is assigned to the 4-proton, strongly deshielded by the peri keto-carbonyl group.\textsuperscript{73}

The 4-protons of the azepines(61) and (63) are also deshielded, though to a lesser extent, by the peri chlorine atom and methoxyl group respectively. The 5-chlorine atom of azepine(61) also deshields the 6-proton, which appears at 2.157 (cf. the unsubstituted azepine(28), in which the 6-proton doublet is centred at 2.327); in contrast, the 6-proton of the azepine(63) is strongly shielded by the 5-methoxy group and appears at 2.87. Such substituent effects are well documented.\textsuperscript{74}

The azepines(68) and (71) and a trace of a blue adduct (p. 143) were obtained from 2-ethylquinoline with dimethyl acetylenedicarboxylate, and the azepine(69)
Figure 1

N.m.r. Spectrum of Azepine (69)
using the diethyl ester. Stubbs also isolated the benzof[\text{\textregistered}] quinolizine (57) and the azepine (70) from the reaction of 2-benzylquinoline with dimethyl acetylene-dicarboxylate during the course of the present investigation.

The u.v. spectra of the azepines (68)-(71) in both neutral and acid solution closely resemble those of (58)-(64) and other azepines under similar conditions,

\begin{align*}
(67) & \\
(68) & \text{R} = \text{Me} \\
(69) & \text{R} = \text{Me}, \text{E} = \text{CO}_2 \text{Et} \\
(70) & \text{R} = \text{Ph}
\end{align*}

and show the presence of the same conjugated system. The n.m.r. spectra of (68)-(70) (Tables 2, 10) all show the expected low-field doublet, assigned to the 6-proton deshielded by the 7-ester group. That of the azepine (69) (Figure 1) shows a high-field AMX\textsubscript{3} system which in (68) is partially obscured by the ester-methyl resonances. No high-field ester group nor high-field aromatic proton is present, thereby excluding the possibility of an ester group at position 11. The only way to accommodate this
Table 2
N.m.r. Spectra of Azepines (68) - (71)

(60MHz, CDCl₃ solution; τ-values, J in Hz)

(68) R = Me
(69) R = Me, E = CO₂Et
(70) R = Ph

(68) ArH(4), 5-H, 2.6-3.0m; 6-H, 2.33d;  J₅, 6 9.5; 10,11-H, 6.0-ca. 6.4m; 11-Me, 8.38d;  J₁₁-H,11-Me 7.6;
ester-Me, 6.23, 6.23, 6.30, 6.37

(69) *Ar-H(4), 5-H, 2.5-3.05m; 6-H, 2.33d;  J₅, 6 9.5; 10-H, 6.14d; 11-H, 6.66m (8 lines); 11-Me, 8.35d;  J₁₀-H,11-H 10.9
J₁₁-H,11-Me 7.7; ester CH₂ 5.6-6.0; ester CH₃, 8.6-8.9

(70) ArH(4), Ph, 2.5-3.1m; 5-H, 3.37d; 6-H, 2.33d;
J₅, 6 9; 10-H, 4.87d; 11-H, 5.39d;  J₁₀,11 10; ester-Me,
5.20, 6.31, 6.59, 6.65

(71) 1-H, 3.52d;  J₁,₂ 8.5; ArH(3), 5-H, 2.62-3.25m; 6-H, 2.45d;  J₅, 6 9.8; 10-H, 6.45-6.96m (8 lines); 10-Me,
8.63d;  J 7.3; 11-H, 5.78d;  J₁₀-H,11-H 9.5; ester-Me,
6.33, 6.33, 6.33, 6.73

* at 100MHz
data in the framework of the chromophore deduced from the u.v. data is to place the AMX$_3$ system as shown. The n.m.r. parameters are normal for such a situation and consistent with those of the azepines lacking the 11-methyl group. The azepine(70) shows the expected AX resonance for the 10- and 11-protons; no marked effect of the 11-phenyl group on other resonances in the molecule could be detected.

The n.m.r. spectrum of the azepine(71) (Tables 2, 10) shows the characteristic high-field ester group (11-ester) and aromatic proton (position 1), and an AMX$_3$ system, visible despite the ester-methyl resonances. The chemical shifts for the AM part of these resonances fit in with those for (29) and (64) and the only structure consistent with the data is that given.

The characteristic feature of the mass spectra of azepines of types (58) and (29) is loss of methyl acrylate from the molecular ion to give the very stable benzo[e]indolizine ion (72), resulting in a base peak.

\[ \text{(72)} \]
at m/e M-86. The azepines (29) and (58)-(64) all display this behaviour. The azepines (68) and (71) give base peaks at m/e M-100, (69) at M-114 and (70) at M-162. These values are interpreted as being due respectively to loss of methyl crotonate, ethyl crotonate and methyl cinnamate. The cracking patterns also show the general features exhibited by the other azepines.\textsuperscript{76}

Oxidation of the 2-methylquinoline azepine (28) with chromic acid gives a product which was assigned the structure (73).\textsuperscript{45} Similar oxidation of the 2-ethyl-

![Image](https://example.com/image.png)

quinoline azepine (68) gave, in very low yield, an oily product whose u.v. was very similar to that of (73). The material could not be induced to crystallise, and unfortunately the n.m.r. spectrum was so poorly resolved that the hoped-for $\text{CHMe}$ pattern, if present, was not distinguishable.

A reaction scheme to account for the formation of the isomeric simple azepines exemplified by compounds (58) and (64) has been proposed (Scheme 3). This scheme,
Scheme 3.

Old Mechanism for Formation of Azepines.

\[ \text{(74)} \]

\[ \text{(75)} \]
which incorporates ideas discussed in Chapter One, requires that the carbon atom of the 2-methyl group of the quinoline nucleus retain its skeletal position in the product and accept a migrating ester group. The isomeric azepines (29) and (64) could be formed as indicated by nucleophilic attack on the other ester group of intermediate (74).

This type of scheme cannot account for the formation of the azepines (68)-(71) and an alternative, which does not involve an ester-shift, is put forward (Scheme 4). This new scheme could apply to the production of simple azepine structures such as (58) and (64) from the appropriate quinoline; the question is discussed below (p. 26).

The essentials of the new proposals are that attack on the acetylenic ester must start from the carbanion (76), which is formed possibly by loss of a proton to a carbanion such as (83) formed in a competing reaction

\[ \text{Scheme 4} \]

\[
\begin{aligned}
\text{CH}_2^+ &\quad \text{E} \\
\text{E} &\quad \text{E} \\
\end{aligned}
\]

\[(83)\]

(cf. the alternative modes of reaction of methyl 2-pyridyl-acetate, p. 9). Formation of the spiro-intermediate (77) and ring-opening in the alternative mode to give (78),

\[
\begin{aligned}
\text{E} &\quad \text{E} \\
\text{CH}_2^+ &\quad \text{E} \\
\end{aligned}
\]

\[(83)\]
Scheme 4.

New Mechanism for Formation of Azepines.
followed by recyclisation and protonation gives (79), corresponding to the adducts (68)-(70). Structure (71) could be formed in a variant of the scheme in which the intermediate (78) cyclises in an alternative fashion yielding the quinolizine (80). A further cyclisation to the cyclopropane (81) followed by ring-expansion and protonation gives the required structural type (82). A cyclopropane intermediate has been put forward to account for the "turning-round" of substituents of a ring in another instance. 19

The fact that the negative charge of the quinolizine (80) does not appear to be stabilised in any way might be considered an objection to the variant scheme. It must also be pointed out however that the isomeric azepines such as (71) are not formed in very good yield; and that different mechanistic schemes may take place concurrently in the reaction mixture, leading to the different products. Thus the formation of the quinolizine (84) in the reaction of 1-methylisoquinoline with dimethyl acetylenedicarboxylate 45 may readily be explained in terms of the old mechanism, as follows, but not in terms of the new mechanism (see next page).

As mentioned above (p. 25), this new scheme could apply equally to the formation of the simple azepines such as (58) and (64), although the older scheme might perhaps be considered more likely. However recent work by Flowerday indicates that the new scheme does apply to the simple azepines.77 The mass spectrum of a sample
of the 2-methylquinoline azepine (28) prepared from 2-\textsuperscript{[13C]}-methylquinoline (11% \textsuperscript{13}C-enrichment) was obtained. If the old scheme operates, the \textsuperscript{13}C is still in its original skeletal position (C\textsubscript{7}) and unlabelled methyl acrylate will be eliminated from the molecular ion, resulting in an enhanced peak at m/e 342 (428-86). But if the new scheme operates, all the \textsuperscript{13}C appears at C\textsubscript{11} and \textsuperscript{13}CH\textsubscript{2}=CH\textsubscript{2} will be eliminated, resulting in no enhancement of the m/e 342 peak (since 428-87=427-86=341). The mass spectrum of the labelled azepine showed (after making the appropriate allowances for the natural abundance of \textsuperscript{13}C) no enhanced peak at m/e 342; hence all the \textsuperscript{13}C was eliminated as acrylate, and all the \textsuperscript{13}C must consequently have migrated from its original position.

A dark green adduct was isolated in very low yield from the reaction of 2,3-dimethylquinoline with dimethyl acetylenedicarboxylate (p. 18). Analysis and the mass
spectrum give a molecular weight of 583, corresponding to a composition of 1 mole quinoline: 3 moles ester. The MX parts of a three-spin AX system are clearly visible in the range 6.6-7.3 ppm of the n.m.r. spectrum; the A part is obscured by the six ester-methyl resonances. The adduct is protonated readily in acid solution, giving rise to a colourless, quinolinium-type chromophore; and the base peak of the mass spectrum occurs at m/e M-86. These data suggest that the compound could be an azepine, with the third mole of ester added in such a way as to extend the conjugated system. Other peaks in the mass spectrum arise from fragmentation of ester-groups, and it does not appear possible to make any worthwhile suggestions regarding the structure in the absence of further chemical evidence.

The reaction of 2-isopropylquinoline with dimethyl acetylenedicarboxylate was investigated in the hope that an azepine, or at least further information regarding the mechanism of azepine-formation, might be obtained. The sole product isolated however was the 4a-isopropyl-4aH-benzo[c]quinolizine (85), whose spectral properties are entirely analogous to those of known 4aH-benzo[c]quinolizines such as (51)-(57). Compound (85) is a thick oil at room temperature, but the 1-isopropyl-1H-benzo[c] quinolizine (86), readily obtained by photolysis of (85), is a crystalline solid. The spectral properties of (86) are again in accord with those of known 1H-benzo[c] quinolizines.
In the n.m.r. spectra of the benzo[c]quinolizines (85) and (86) the isopropyl group methyl resonances do not appear as simple 6-proton doublets. Two doublets, their centres separated by ca. 2 Hz, appear in each spectrum. The isopropyl methyl groups are diastereotopic, and the difference in magnetic environments must be sufficient for non-equivalence to be observed in both cases.

The initial step in the new mechanism proposed for azepine-formation is loss of a proton to give the carbanion intermediate (76). Loss of a proton from 2-isopropylquinoline to give the analogous carbanion (87) is likely to occur less readily because of the destabilising effect of two electron-donating methyl groups on this carbanion. Thus, in terms of the new mechanism for
azepine-formation, the fact that 2-isopropylquinoline does not give rise to an azepine may well reflect this decrease in the acidity of the active hydrogen atoms of the 2-substituent.
Chapter 3

The "Red" Adducts from Substituted 2-Methylquinolines
and Dimethyl Acetylenedicarboxylate.
Two red adducts are formed in the reaction of 2-methylquinoline with dimethyl acetylenedicarboxylate. 2,8-Dimethylquinoline with this ester also gives two red adducts, shown on the basis of spectral evidence to be analogues of the 2-methylquinoline red adducts. As mentioned previously (p. 14), Gagan\textsuperscript{70} reported the isolation of only one red adduct from each of these reactions, but Caterer\textsuperscript{71} appears to have been aware that two red adducts are formed from 2-methylquinoline. Further confusion has also arisen in the past because when Diels first isolated the adduct now known to be the 2-methylquinoline azepine(28), he described it as a red compound.\textsuperscript{80} The azepine(28) is orange, but Diels' sample was probably contaminated with the "red" adduct(s) discussed in this chapter. Gagan, before discovering the true colour of the azepine, employed the description "dark red" for these more complex adducts,\textsuperscript{70} but now the term "red" is sufficient.

Acetonitrile, although a good solvent for ester reactions, is not a convenient solvent for the preparation of pure samples of the 2-methyl- and 2,8-dimethyl-quinoline red adducts. On the alumina chromatography columns used to separate the components of the reaction mixtures, the yellow-orange azepine bands merge into the red adduct bands, with the result that an appreciable proportion of the total amount of red adduct(s) is isolated as an azepine-red adduct(s) mixture. A second, far more serious disadvantage is that these red bands
yield mixtures of the two red adducts which cannot be separated by fractional crystallisation. In this context it seems very surprising that Gagan obtained pure samples of only one red adduct from both 2-methyl- and 2,8-dimethylquinoline.

Dry methanol however is an excellent solvent for these reactions, both disadvantages being circumvented by its use. In methanol the red and blue adducts are the sole products (apart from ester polymer) from 2-methyl- and 2,8-dimethyl-quinoline with dimethyl acetylenedicarboxylate, and thus there are no problems of separation. Also, as the reaction in methanol proceeds, dark crystals separate from the tarry solution. In the case of 2-methylquinoline these crystals, after chromatography on alumina, yield a pure sample of Gagan's red adduct and also some blue adduct. With 2,8-dimethyl-quinoline, simple recrystallisation of the dark crystals gave a pure sample of Gagan's red adduct. The tarry supernatants in both cases yield the mixed red adducts and the blue adducts after chromatography on alumina. This method suffers from the disadvantage that much tar is formed in the reaction; it is also a wasteful preparation, typical net yields of pure, single red adduct being 3% (2-methylquinoline) and 8% (2,8-dimethylquinoline). However it is the only way so far discovered of obtaining pure samples of Gagan's red adducts in experimentally useful amounts. Pure samples of the isomeric red adducts have not been isolated in this investigation, although
it seems likely that small amounts could be obtained by preparative thin layer chromatography of the red-adduct mixtures.

For convenience, the red adducts isolated by Gagan will be termed the "first" red adducts; the isomeric red adducts not reported by Gagan will be termed the "second" red adducts.

The only other quinoline which was found to yield analogous red adducts was 2,6,8-trimethylquinoline; reaction with dimethyl acetylenedicarboxylate in acetonitrile gave two red adducts which could be separated by chromatography on alumina. These are, on the basis of spectral evidence, analogues of the first and second red adducts from 2-methyl- and 2,8-dimethyl-quinoline. A dark red compound isolated from the reaction of 2,4-dimethylquinoline with the methyl ester in methanol is discussed on p. 51.

It is now proposed that the first and second red adducts from 2-methyl-, 2,8-dimethyl- and 2,6,8-trimethyl-quinoline are geometric isomers of the 9-azacyclopenta[a]phenanthrene structures (88), (89) and (90) respectively.* Analysis and mass spectra of the four red adducts obtained pure (viz. the 2-methyl- and 2,8-dimethyl-quinoline first red adducts and the two 2,6,8-trimethylquinoline red adducts) confirm the

---

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar-H</th>
<th>7,6-H</th>
<th>17-H</th>
<th>11,12-H</th>
<th>ester-Me</th>
</tr>
</thead>
<tbody>
<tr>
<td>(88a)</td>
<td>2.7-</td>
<td>2.99d, 3.45d</td>
<td>4.41</td>
<td>3.1</td>
<td>J 10.4</td>
</tr>
<tr>
<td></td>
<td>3.1</td>
<td></td>
<td></td>
<td>5.12d</td>
<td>6.20d</td>
</tr>
<tr>
<td>(89a)</td>
<td>2.7-</td>
<td>2.99d, 3.46d</td>
<td>4.51</td>
<td>3.2</td>
<td>J 10.0</td>
</tr>
<tr>
<td></td>
<td>3.10</td>
<td>3.03d, 3.46d</td>
<td>4.55</td>
<td>3.13</td>
<td>J 10.0</td>
</tr>
<tr>
<td></td>
<td>3.1</td>
<td></td>
<td></td>
<td>5.47d</td>
<td>5.84d</td>
</tr>
<tr>
<td>(88b)\text{a}</td>
<td>2.6-</td>
<td>2.89d, 3.46d</td>
<td>4.81</td>
<td>3.1</td>
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<td>3.1</td>
<td></td>
<td></td>
<td>5.47d</td>
<td>5.84d</td>
</tr>
<tr>
<td>(89b)\text{b}</td>
<td>2.7-</td>
<td>?, 3.41d</td>
<td>4.95</td>
<td>3.2</td>
<td>J 10.5</td>
</tr>
<tr>
<td>(90b)\text{*}</td>
<td>3.08</td>
<td>2.95d, 3.36d</td>
<td>4.95</td>
<td>10.0</td>
<td>J 12.0</td>
</tr>
</tbody>
</table>

* at 100MHz

\text{a} Values obtained from spectrum of a fairly pure sample recovered after an unsuccessful reaction starting with red-adduct mixture.

\text{b} Values obtained from spectrum of red-adduct mixture.
composition 1 mole quinoline: 3 moles ester.

The n.m.r. spectra of the red adducts from 2-methylquinoline (Tables 3,10) show the presence of four aromatic protons; likewise the spectra of the adducts from 2,8-dimethyl- and 2,6,8-trimethyl-quinoline show the presence of three and two aromatic protons respectively. The two protons at positions 3 and 4 of the original quinoline ring are visible in all cases, and thus the remainder of the structure must occur at positions 1 and 2 of the quinoline. Two one-proton doublets and a one-proton singlet are also present in all cases in the range 4 - 6r. These data lead to a number of possible structures, as well as excluding many others; the structures (88) - (90) appear to be most likely and are used as the basis of the present discussion. Other, less likely structures are discussed on p. 53.
Figure 2

N.m.r. Spectra of the 2,6,8-Trimethylquinoline Red Adducts

first

second

\[ \text{CHCl}_3 \]
The n.m.r. spectra give an immediate means of classifying the red adducts as "first" red adducts (structures (88a)-(90a)) and "second" red adducts (structures (88b)-(90b)). The first red adducts show a one-proton singlet at ca.4.5\(\tau\), assigned to the 17-proton, and doublets at ca.5.1 and 6.1\(\tau\) assigned to the 11- and 12-protons respectively (see below). The 17-proton of the second red adducts however appears at ca.4.9\(\tau\), and the 11- and 12-proton doublets at ca.5.3 and 5.7\(\tau\). These differences are clearly exemplified by the spectra of the two red adducts from 2,6,8-trimethylquinoline reproduced in Figure 2.

The doublets at ca.2.9 and 3.4\(\tau\) are assigned to the 7- and 6-protons respectively, the 7-proton being deshielded to some extent by the 15-ester group. It does appear necessary to postulate this deshielding effect, which is similar to that observed in the azepines (Chapter 2). Tully isolated compounds such as (91) and (92) in which the ester group attached to the carbon atom adjacent to

![Diagram of structures (91) and (92)]
### Table 4

**N.M.R. Spectra of the Red Adducts in T.F.A. Solution**

<table>
<thead>
<tr>
<th>Compound</th>
<th>$J_{1-H}$</th>
<th>$J_{11-H}$</th>
<th>$J_{12-H}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(88a)</td>
<td>2.19d</td>
<td>1.48-2.0</td>
<td>4.54d</td>
</tr>
<tr>
<td>(89a)</td>
<td>-</td>
<td>1.6-2.1</td>
<td>4.98d</td>
</tr>
<tr>
<td>(90a)</td>
<td>1.5-2.1</td>
<td>2.0</td>
<td>5.59d</td>
</tr>
<tr>
<td>(88b)</td>
<td>1.2</td>
<td>-</td>
<td>4.74d</td>
</tr>
<tr>
<td>(89b)</td>
<td>1.98-2.15</td>
<td>7-H, 1.86d</td>
<td>4.98d</td>
</tr>
<tr>
<td>(90b)</td>
<td>2.1</td>
<td>1.01d</td>
<td>4.98d</td>
</tr>
</tbody>
</table>

- *Obscured by ester-Me resonances.*
- *Obtained from spectrum of red-adduct mixture; other resonances not distinguishable from those of first red adduct (89a).*
- *Apparent singlet.*

<table>
<thead>
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<th>$J_{12-H}$</th>
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<tr>
<td>(90a)</td>
<td>1.5-2.1</td>
<td>2.0</td>
<td>5.59d</td>
</tr>
<tr>
<td>(88b)</td>
<td>1.2</td>
<td>-</td>
<td>4.74d</td>
</tr>
<tr>
<td>(89b)</td>
<td>1.98-2.15</td>
<td>7-H, 1.86d</td>
<td>4.98d</td>
</tr>
<tr>
<td>(90b)</td>
<td>2.1</td>
<td>1.01d</td>
<td>4.98d</td>
</tr>
</tbody>
</table>

- *Obscured by ester-Me resonances.*
- *Obtained from spectrum of red-adduct mixture; other resonances not distinguishable from those of first red adduct (89a).*
- *Apparent singlet.*
the nitrogen atom deshields the peri aromatic proton; the steric requirements for this deshielding effect are met in the case of the red adducts.

The first red adducts show one high-field ester-methyl resonance, assigned to the 11-ester methyl group which is shielded by the benzo-ring as in certain of the azepines (Chapter 2). The 1-proton of the 2-methylquinoline first red adduct is not however strongly shielded by the 11-ester group; it probably occurs at ca. 2.9 T. In Tully's azepine (91), the 1-proton, shielded by the 10-ester group, appears at only 3.10 T; the 10-ester methyl is thought to occur at 6.54 T. The extent of the shielding effect thus appears to depend very much on the precise stereochemistry of the molecule, as is fully expected.

The n.m.r. spectra of the 2-methylquinoline red adducts in trifluoroacetic acid solution (Tables 4, 10) confirm this smaller shielding effect. The spectrum of the first red adduct shows a doublet at 2.1 T (J 8.5 Hz, further split), upfield from the other aromatic proton resonances, which is assigned to the 1-proton; however the 1-proton signal of the second red adduct from 2-methylquinoline is buried in the aromatic-proton multiplet, 1.3-1.95 T. The spectrum of the first red adduct from 2,8-dimethylquinoline shows no upfield doublet in the aromatic region, as is expected because of the presence of the methyl group at position 1.

The adducts are protonated in trifluoroacetic acid
solution to give yellow species assigned structures such as \((93)\). The 6-protons appear as very low-field doublets, characteristic of the quinolinium nucleus (cf. the spectra of azepines (Chapter 2) in trifluoroacetic acid solution.) There are no one-proton singlets in the range 2.5-5.5\(\tau\); instead the 17-proton signal, with that of the added 16-proton, is now obscured by the ester-methyl resonances. Comparison of the spectra run in deuteriochloroform and trifluoroacetic acid solution suggests that the lower doublets of the mid-field AX quartets must be assigned to the 11-protons and the higher to the 12-protons. In trifluoroacetic acid solution the 11-proton, adjacent to the positively-charged nitrogen atom, would certainly be expected to appear downfield from the 12-proton; a downfield shift of ca.0.5\(\tau\) on changing from deuteriochloroform to trifluoroacetic acid as solvent is then indicated in the case of the first red adducts. The 12-protons are moved downfield by only ca.0.3\(\tau\) in these adducts, which is consistent with their being further removed from the nitrogen atom. However
the 11- and 12-protons of the second red adducts from 2,8-dimethyl- and 2,6,8-trimethyl-quinoline appear as 2-proton singlets at ca. 5.0r in trifluoroacetic acid solution, presumably as a result of conformational changes on protonation. The above assignments then require that the 12-proton move further downfield than the 11-proton on changing from deuteriochloroform to trifluoroacetic acid as solvent, and so the assignments for these two second red adducts in deuteriochloroform solution could be reversed. The second red adduct from 2-methylquinoline does not exhibit this effect.

The spectra of the second red adducts show no upfield ester-methyl resonance; this observation, along with the lack of shielding of the 1-proton of the 2-methylquinoline adduct, indicates that the 11-ester group is well removed from the vicinity of the benzo-ring. The 11- and 12-ester groups are expected to be trans to one another; steric crowding would make cis ester groups most unlikely. It is difficult to define the stereochemistry of the C\textsubscript{11}-C\textsubscript{13},C\textsubscript{17} saturated system; inspection of models indicates that the dihedral angle between the C\textsubscript{11}- and C\textsubscript{12}-protons could fall within the approximate range 130°-170° (assuming trans ester groups), which is consistent in terms of Karplus's theory with the observed values of J\textsubscript{11,12}. Variations in the stereochemistry of the various molecules are reflected in differences between the values of J\textsubscript{11,12} observed for different adducts, and for a given adduct in deuteriochloroform and trifluoroacetic acid solution.
The u.v. spectra of the red adducts in neutral solution show complex absorption bands in the visible region. The conjugated chromophore of the structures (88) - (90) contains the same number of double-bonds as that of the azepines discussed in Chapter 2, and yet the azepines absorb at somewhat lower wavelengths in the visible region. Inspection of a model of the red adduct structure indicates that the complete conjugated system is fairly rigid and planar, permitting good π-orbital overlap. Not much is known about the conformation of the azepine ring, but it seems very likely that the ring is flexible and the double-bond system non-planar; π-orbital overlap cannot then be as effective as in the rigid red-adduct structure and absorption will occur at shorter wavelengths.

The u.v. spectra of the three first red adducts are very similar; slight differences between the spectra of the first and second red adducts from 2,6,8-trimethyl-quinoline are attributable to the effect of differences in molecular geometry on the conjugated chromophore. In acid solution the adducts protonate readily to give the yellow species such as (93); again, differences in molecular geometry explain slight differences in the spectra of the two 2,6,8-trimethyl-quinoline adducts. The u.v. spectra of the protonated red adducts are unlike those of the protonated azepines (Chapter 2); the latter give colourless, quinolinium-
type spectra, whereas the yellow colour of the protonated red adducts shows the presence of a more conjugated chromophore.

The base peaks of the mass spectra (Table 111) of the pure red adducts all occur at an $m/e$ value of $M-144$, corresponding to loss of dimethyl fumarate (or maleate). Caterer noted that the strong peaks observed in the mass spectrum of dimethyl fumarate (viz. $m/e$ 114, 113, 85, 59) also occur in the mass spectra of the first red adducts from 2-methyl- and 2,8-dimethyl-quinoline; these peaks also occur in the spectra of the other pure adducts isolated. The elimination of fumarate (maleate) is readily accounted for by the electrocyclic process indicated. Loss of an ester group also occurs from the molecular ion; the angular 13-ester group is most likely the group in question, resulting in the formation of the
stable quinolinium species (95). The mass spectra of the two 2,6,8-trimethylquinoline adducts are very similar.

Treatment of the first red adduct from 2-methylquinoline with bromine in boiling glacial acetic acid gave a yellow monobromo- derivative, assigned the quinoline structure (96), and dimethyl fumarate. The single proton in the cyclopentadienyl ring of compound (96)

![Chemical Structure](image)

(96)

could, by an appropriate series of [1,5] thermal shifts, be present at any position in the ring; however the fully-conjugated structure shown is preferred on grounds of stability and colour. 2-Substituted quinolines in which only one conjugated double-bond is present in the substituent are colourless (e.g.p. 58).

The u.v. spectrum of the quinoline (96) is unchanged in even strongly-acid solution, in keeping with its quinoline structure. In the n.m.r. spectrum deshielding of the 5-proton by the peri bromine atom is apparent. The cyclopentadienyl ring proton appears in the aromatic region; the spectrum in trifluoroacetic acid solution
Figure 3

Mass Spectra of Compounds (88a) and (97)
shows a singlet at 2.43Å, assigned to this proton.

Debromination of the bromo-compound (96) with hydrogen and palladium-on-charcoal gave the quinoline (97). This compound was also obtained directly as a product of the reaction of the first red adduct from 2-methylquinoline with zinc in glacial acetic acid. The 5-proton is no longer deshielded in this compound, and the n.m.r. spectrum in trifluoroacetic acid solution shows clearly the 3- and 4-proton doublets at 2.04Å and 0.86Å respectively. The cyclopentadienyl ring proton appears at 2.43Å in this solvent, confirming the assignment in the case of the bromo-compound.

The cracking pattern of the mass spectrum of the quinoline(97) (Figure 3) is very similar to that of the parent red adduct in the range below m/e 425(N-144). Likewise the bromo-derivative(96) gives a cracking pattern very similar to that of compound(97), except that the spectrum consists of isotopic doublets 79 and 81 mass units above the corresponding peaks in the spectrum of compound (97). It thus appears that the red adduct structure readily eliminates dimethyl fumarate (or maleate)
either in the course of a chemical reaction or in the mass spectrometer; as stated, dimethyl fumarate was isolated from the bromination reaction mixture. The intermediate ion (94) shown in the scheme of the mass spectrum of the red adduct structure on p. 41 might thus well be rewritten as (98). The formation of compound (98) and dimethyl fumarate (not isolated) in the reaction with zinc in acetic acid does not constitute an overall reduction; nor does the bromination reaction result in oxidation (except at the 4-position of the quinoline nucleus). These reactions, and the fragmentation in the mass spectrometer, are electrocyclic rearrangements which result in elimination. This facile elimination of fumarate (maleate), more particularly when considered in conjunction with the shielding effects observed in the n.m.r. spectra, provides good evidence in favour of a red-adduct structure involving a saturated -CHE-CHE- grouping attached to the nitrogen atom.

The introduction of a bromine atom to give compound (96) appears to be an independent substitution reaction, for which the following mechanism is suggested. The
initial attack by bromonium ion is analogous to

\[
\begin{align*}
\text{(86)} \\
\begin{array}{c}
\text{N} \\
\text{H} \\
\text{E}
\end{array}
\end{align*}
\]

protonation (p. 38); then nucleophilic attack by bromide ion at the 4-position of the quinoline nucleus occurs, followed by elimination of the elements of hydrogen bromide to give the bromo-intermediate (99). The elimination of fumarate (maleate) seems likely to occur as a subsequent step. Taylor\(^8\) and Acheson and Snaith\(^8\) have reported comparable reactions in the indole series which involve a similar sequence of electrophilic followed by nucleophilic attack.

Compound (97) reacts with diazomethane to give a
crystalline substance which was shown by elemental analysis to have the molecular formula $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_8$ (M.W. 467). The substance melts with evolution of a gas, presumably nitrogen. These results indicate that the substance is a pyrazoline, formed by attack of diazomethane at an olefinic double-bond; assuming structure (97), the pyrazoline structures (100) and (101), formed by attack at the less-hindered double bond, appear plausible.

The integral of the n.m.r. spectrum of the substance shows clearly the presence of six aromatic protons, thereby excluding the possibility of a pyrazoline such as (102), formed by attack on the quinoline nucleus. The n.m.r. spectrum also shows what appear to be two quartets in the region 4.4-5.4 ppm, the complete pattern integrating.
to two protons. This possibly indicates that the substance is a mixture of racemates, or a mixture of isomers such as (100) and (101), the two quartets arising from two sets of non-equivalent ring methylene protons.

The substance gives an extremely weak molecular ion in the mass spectrum; the base peak occurs at \( m/e 439(M-28) \), as a result of loss of a molecule of nitrogen. As expected, this mass spectrum is virtually identical to that of the material obtained by pyrolysis of the pyrazoline; on melting the pyrazoline presumably forms a cyclopropane with evolution of nitrogen. Feinberg reported an analogous reaction sequence, starting with the "first stable adduct" (103) from stilbazole and dimethyl acetylenedicarboxylate.

Reaction of the first red adduct from 2,8-dimethyl-quinoline with bromine in acetic acid gave in very low yield a pale yellow substance whose u.v. spectrum is very similar to that of the bromo-compound(96). The n.m.r. spectrum however, whilst appearing quite similar
to that of compound (96), shows a cluster of ester-methyl resonances, and four other peaks in the range 6.7-7.5 τ, indicating that the substance is probably a mixture of compounds analogous to compound (96) resulting from further bromination of the benzo-ring methyl group. No pure compounds could be isolated from the reaction of the red adduct with zinc in acetic acid.

On stirring methanolic solutions of the first red adducts from 2-methyl- and 2,8-dimethyl-quinoline with 4% sodium amalgam, yellow solutions were obtained; however no tractable products were isolated from these reactions. An attempt to oxidise the first red adduct from 2-methyl-quinoline with 2N nitric acid likewise gave no tractable product. In an attempt to methylate the cyclopentadienyl ring, compound (97) was treated with sodium hydride and methyl iodide in dry ether; starting-material was recovered.

The quinolines (96) and (97), in company with certain other substituted quinolines (p. 47), do not form methiodides on treatment with methyl iodide in boiling acetonitrile. In the case of compounds (96) and (97) this is unlikely to be a steric effect; it presumably reflects a decrease in the nucleophilic strength of the nitrogen atom resulting from conjugation with substituents on the cyclopentadienyl ring.

Gagan described colourless hexahydro-derivatives of the first red adducts from 2-methyl- and 2,8-dimethyl-quinoline, 70 and a yellow tetrahydro-derivative of the 2-methylquinoline adduct. 45, 70 His method of hydrogenation
<table>
<thead>
<tr>
<th>Compound</th>
<th>$\lambda_{\text{max}}$ (nm)</th>
<th>$10^{-4}\varepsilon$ (in methanol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(104)</td>
<td>259 (0.89), 299 (0.18)</td>
<td></td>
</tr>
<tr>
<td>(105)</td>
<td>219 (1.25), 264 (0.50), 297 (0.12)</td>
<td></td>
</tr>
<tr>
<td>(106)</td>
<td>271 (1.47), 282 (1.57)</td>
<td></td>
</tr>
<tr>
<td>N,N-diethyl-aniline</td>
<td>260 (1.62), 303 (0.23)</td>
<td></td>
</tr>
<tr>
<td>(107)</td>
<td>301 (1.62)</td>
<td></td>
</tr>
<tr>
<td>(108)</td>
<td>238 (1.95), 289 (0.50)</td>
<td></td>
</tr>
</tbody>
</table>
involved shaking methanolic suspensions of the adducts under hydrogen in the presence of palladium charcoal or Adams' catalyst. Since the adducts are only sparingly soluble in methanol this method is very unsatisfactory; however glacial acetic acid was found to be an excellent solvent for these hydrogenation reactions.

Hydrogenation of the first red adduct from 2-methylquinoline in glacial acetic acid in the presence of Adams' catalyst gave Gagan's hexahydro-derivative; a new, colourless tetrahydro-derivative was obtained with 5% palladium-on-charcoal. A small amount of Gagan's hexahydro-derivative was isolated by hydrogenation of a mixture of the red adducts from 2,8-dimethylquinoline in methanol using Adams' catalyst. The hexahydro-derivatives of the first red adducts from 2-methyl- and 2,8-dimethylquinoline are assigned structures (104) and (105) respectively, and the new tetrahydro-derivative of the 2-methylquinoline adduct, structure (106).

![chemical structures](image)

(104)  (105) 1-Me

(106)
Table 6
N.m.r. Spectra of Hydrogenated Red Adducts

(60MHz, CDCl₃ solution; τ-values, J in Hz)

\[ \text{Spectra of Hydrogenated Red Adducts} \]

\[ (104) \]

\[ (105) \]

\[ (106) \]

\[ (104) \]

1-H, 3.81d; \( J \), 7.6; 2,3,4-H, 3.0-3.6m; aliphatic H(11), 5.7-7.95m; ester-CH₃, 6.32-6.40(15), 6.92

\[ (105) \]

1-Me, 7.90; 2,3,4-H, 3.1-3.4m; aliphatic H(11), 5.6-8.1m; ester-CH₃, 6.33-6.40(15), 7.03

\[ (106) \]

1-H, 3.76d; \( J \), 2.80; 2,3,4-H, 2.9-3.55m; 11(?)-H, 5.29d, \( J \), 8.8; aliphatic H, 5.9-7.14m(4) and 7.31br(4); ester CH₃, 6.30-6.38(15), 6.73

Gagan's tetrahydro-derivative from the 2-methylquinoline first red adduct:

\[ \text{ArH(4), 2.7-3.4m; aliphatic H, 5.59d(1), J 10.0;} \]
\[ 6.06-6.6(2);^a 6.8-7.4m(4); 7.5-8.0m(2); \text{ester-CH₃(18), 6.1-6.5} \]

^a Almost totally obscured by ester-methyl resonances.
The u.v. spectra (Table 5) of the hexahydro-derivatives (104) and (105) are very similar to the spectrum of N,N-diethylaniline;\(^8\) the u.v. spectrum of the tetrahydro-derivative (106) shows less conjugation than that of ethyl \(\beta\)-anilinocrotonate (107) or the addition compound (108) from N-methylaniline and dimethyl acetylenedicarboxylate.\(^6\) The n.m.r. spectra (Table 6) of the 2-methylquinoline red adduct derivatives both show upfield ester-methyl resonances, assigned as with the parent red adducts to the 11-ester methyl groups, and only four aromatic protons, one of which appears as a high-field doublet. This is assigned to the 1-proton as before; the stereochemistry of the molecules seemingly permits much greater shielding of this proton in these derivatives than in the parent adduct. The spectrum of the hexahydro-derivative (105) from 2,8-dimethylquinoline also shows a high-field ester-methyl resonance, but only three aromatic protons; as expected, there is no high-field doublet in the aromatic region. The mass spectra of these derivatives all show fragment ions at \(m/e\) \(X-144;\)
Scheme 5.
Mechanism for Formation of the Red Adducts.

(109)
however fragmentation of ester groups is the dominant feature of these spectra.

The yellow tetrahydro-derivative of the 2-methyl-45,70-quinoline first red adduct reported by Gagan was not isolated in this investigation. Gagan's n.m.r. spectrum shows no high-field ester-methyl or aromatic proton resonances, but his mass spectrum is almost identical to that of the tetrahydro-derivative (106); his compound therefore is possibly a geometric isomer of compound (106).

A reaction scheme to account for the formation of the red adducts is proposed (Scheme 5). This involves a familiar pattern of carbanion-formation and Michael addition and is consistent with the formation of isomeric first and second red adducts. The stereochemistry of the various double-bonds and of the cyclisations indicated for the intermediate (109) allows ample opportunity for such formation of geometric isomers. Several of the stages indicated could be concerted; equally, the cyclisations of the intermediate (109) need not be concerted although they are shown as such.

A red-coloured adduct isolated in very low yield from the reaction of 2,4-dimethylquinoline with dimethyl acetylenedicarboxylate in methanol is assigned the structure (110). No other tractable products were isolated from this reaction, and a very great deal of tar was formed. The n.m.r. spectrum of this adduct shows the characteristic features of a "second" red adduct; in addition there are
resonances due to two extra ester-methyl groups, a methylene group and an olefinic proton, and there is no aromatic-methyl resonance. The methylene resonance is buried in the ester region (6.1-6.5τ); this is markedly upfield from the position of the methylene resonance in the adduct (39) and analogues (p. 58) (ca. 5.5τ) and appears to exclude the isomer in which the side-chain double-bond is conjugated with the ring (cf. a fuller discussion of a similar instance, p. 59). The olefinic proton resonance at 3.63τ is then assigned to the side-chain maleate proton, although a fumarate side-chain is by no means excluded (cf. p. 60).

The 4-methyl group of 2,4-dimethylquinoline is activated as well as the 2-methyl group, and the formation of this
adduct is thus comparable to the formation of the compound (39) and analogues by attack initiated from activated 2-methyl groups. A further example of attack apparently initiated from an activated 4-methyl group is discussed on p. 59.

The u.v. spectrum of the adduct (110) is very similar to that of the second red adduct from 2-methylquinoline, and the pattern of fragmentation in the mass spectrometer is also very similar to that of the other red adducts.

Mention will now be made of two alternative structures for the red adducts, and the principal reasons for rejecting them. The structure (111) is compatible with the n.m.r. spectrum in deuteriochloroform solution of the first red adduct from 2-methylquinoline. On this basis
the second red adduct, with the olefinic-proton singlet at higher field, would be assigned the corresponding N-maleate structure (cf. p. 61). However the structure (111) would on protonation give the species (112), which would still show an olefinic proton in the n.m.r. spectrum. As discussed above (p. 38), no such olefinic proton resonances are visible in the n.m.r. spectra of the red adducts in trifluoroacetic acid solution. Furthermore the shielding effects observed in the case of the first red adducts (p. 37) cannot be so easily explained in terms of structure (111), although inspection of a model indicates that the β-ester methyl group could possibly be situated above or below the benzo-ring.

Elimination of fumarate (maleate) from structure (111), while being plausible, is less facile than in the case of the assigned structure.

On the basis of structure (111), the tetrahydro- and hexahydro-derivatives of the first red adduct from 2-methylquinoline would be assigned the structures (113) and (114) respectively, assuming in each case that the
least-hindered double bonds are preferentially reduced. The hexahydro-structure \((114)\) incorporates an \textit{exo} double-bond at the 2-position of the quinoline nucleus, giving a degree of conjugation which is incompatible with the observed u.v. spectrum \((\text{cf.} p. 50)\). Again, the shielding of an ester-methyl group and an aromatic proton observed in the n.m.r. spectra of both derivatives of the 2-methylquinoline adduct are much less satisfactorily explained by these alternative structures.

The variant structure \((115)\) for the first red adduct from 2-methylquinoline is equally open to all of the above objections. A deshielding of the proton at position 3 of the quinoline ring would be postulated \((\text{cf.} p. 36)\) in this case, but not in the case of structure \((113)\); this would however lead merely to an inversion of the assignments of the chemical shifts of the 3- and 4-protons.

Structure \((116)\) for the first red adduct from 2-methylquinoline is highly conjugated, although the degree of planarity of the complete conjugated chromophore is
uncertain. Elimination of fumarate (maleate) does not appear to be very favourable; furthermore a cyclisation step would then be necessary to give the appropriate 2-substituted quinoline. The tetra- and hexahydro-derivative would be assigned the structures (117) and (116) respectively; again the structure (118) is not compatible with the observed u.v. spectrum.

As stated above, the red adducts discussed in this chapter are the only red adducts to have been isolated in manageable yield. It appears likely that any 2-methyl-
quinoline with further substituents in the benzo-ring will form red (and blue) adducts; a red adduct mixture has recently been isolated using 6-bromo-2-methylquinoline. The failure of 2,3-dimethylquinoline to form red and blue adducts is attributable to steric crowding caused by the 3-methyl group. There appears however to be no obvious reason why 2,4-dimethyl- and 4-chloro-2-methyl-quinoline do not react in the same manner as 2-methyl-quinoline; it is conceivable that this reflects delicate electronic effects on the course of reaction.

The fact that no benzo[c]quinolizines and azepines are formed when reaction is carried out in methanol is also very surprising. The mechanisms proposed for the formation of these adducts are very similar in nature to that proposed for the formation of the red adducts, and there thus appears to be no simple explanation of this phenomenon.
Chapter 4

Other Adducts from Substituted 2-Methylquinolines and Dimethyl Acetylenedicarboxylate.
Certain other adducts isolated from the reactions of various substituted 2-methylquinolines with dimethyl acetylenedicarboxylate are discussed in this chapter.

As mentioned previously (p. 16) the quinoline (31) is the sole product of the reaction of 8-bromo-2-methylquinoline with the ester. The analogues (119), (120) and (121) were isolated from the reactions of the ester with 2,8-dimethylquinoline, 2,6,8-trimethylquinoline and 2,4,6,8-tetramethylquinoline in acetonitrile respectively. The u.v. spectra of these adducts show clearly, on comparison with those of the parent quinolines, an increase in conjugation; the double-bond is thus conjugated with the ring as shown (cf. p. 59). In the n.m.r. spectra the side-chain vinyl proton and methylene protons appear as sharp singlets at ca. 2.1 and 5.57 respectively (CDCl₃ solution).

The τ-values of the aromatic-methyl resonances in
### Table 7

Methylquinolines: \( \tau \)-Values of Methyl Groups in T.F.A. Solution.

<table>
<thead>
<tr>
<th>Compound</th>
<th>2,4-Me</th>
<th>6-Me</th>
<th>8-Me</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-methylquinoline</td>
<td>6.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2,4-dimethylquinoline</td>
<td>6.94, 6.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2,6-dimethylquinoline</td>
<td>6.94</td>
<td>7.30</td>
<td></td>
</tr>
<tr>
<td>2,8-dimethylquinoline</td>
<td>6.85</td>
<td></td>
<td>7.11</td>
</tr>
<tr>
<td>2,6,8-trimethylquinoline</td>
<td>6.90</td>
<td>7.36</td>
<td>7.14</td>
</tr>
<tr>
<td>2,4,6,8-tetramethylquinoline</td>
<td>6.95, 6.98</td>
<td>7.34</td>
<td>7.14</td>
</tr>
<tr>
<td>(119)</td>
<td></td>
<td></td>
<td>7.07</td>
</tr>
<tr>
<td>(120)</td>
<td></td>
<td></td>
<td>7.10</td>
</tr>
<tr>
<td>(121)</td>
<td>6.93</td>
<td>7.31</td>
<td>7.16</td>
</tr>
<tr>
<td>(122)</td>
<td>6.92( ^\text{a} )</td>
<td>7.38</td>
<td>7.16</td>
</tr>
<tr>
<td>(124)</td>
<td>6.91</td>
<td>7.29</td>
<td>7.16</td>
</tr>
</tbody>
</table>

All spectra measured at 60MHz.

\( ^\text{a} \) uncertain whether 2- or 4-Me.
these and other quinolines may be assigned by a correlation of the appropriate spectra obtained in trifluoroacetic acid solution (Table 7). This method does not distinguish between 2- and 4-methyl groups; however the structure (121) is assigned to the 2,4,6,8-tetramethylquinoline adduct (rather than a structure with the side-chain at position 4) since the adduct, whose formation would be expected, appears to be in all respects analogous to the adducts (39), (119) and (120).

An isomer of the adduct (121) isolated in very low yield from the reaction of 2,4,6,8-tetramethylquinoline with the ester is assigned the structure (122). The u.v. spectrum of this adduct shows slightly more conjugation

![Molecular structure of (122) and (123)]

than that of 2,4,6,8-tetramethylquinoline but appreciably less than that of adduct (121). Furthermore the methylene protons appear in the n.m.r. spectrum as a singlet at 6.71\(^{\text{H}}\), which is close to the position of the methylene resonance
of 2-ethylquinoline (quartet centred at 7.07, in CDCl₃ solution). A one-proton singlet at 2.95T is assigned to the side-chain fumarate proton. The side-chain is considered to be the fumarate rather than the maleate since maleate protons, not being deshielded by a cis ester-carbonyl group, appear at nearer 4T (cf. p. 61); for example the olefinic protons of diethyl fumarate appear at 3.17T while those of diethyl maleate appear at 3.72T. A broad one-proton singlet at 1.84T is assigned to the 5-proton, apparently strongly deshielded by the 4-side-chain. Although all types of substituents cause deshielding of peri protons, the extent of deshielding in this particular case would appear to be surprisingly large. The alternative structure (123) with a non-conjugated side-chain at position 2 is not excluded by these data; the singlet at 1.84T would then be assigned to the 3-proton. This deshielding effect however appears to be even less plausible than the previous one.

In trifluoroacetic acid solution the resonances are moved down-field by amounts in the range 0.2-0.8T. The adduct was recovered unchanged from this solvent, although acid-catalysed isomerisation to a fully-conjugated structure might have been expected.

A third colourless adduct isolated from the reaction of 2,4,6,8-tetramethylquinoline with dimethyl acetylene-dicarboxylate is assigned the structure (124). The alternative structure (125) is not excluded and is discussed on p. 62, but structure (124) is used as the
basis of the present discussion. No analogues were obtained from any other 2-methylquinolines. The u.v. spectrum of this adduct is essentially that of a quinoline and is only slightly changed in acid solution. The n.m.r. spectrum shows an olefinic-proton singlet at 4.74\(\tau\) (CDCl\(_3\) solution), and hence the adduct is considered to be the O-maleate rather than the O-fumarate. The olefinic protons of N- and O-fumarates and -maleates appear at higher field than those of simple fumarates and maleates because electron-donation from the hetero-atom results in a shielding effect; again however it is generally possible to distinguish between corresponding fumarates and maleates, the protons of the former appearing at lower field. An O-fumarate would be expected to show a proton-resonance near 4\(\tau\).

The chemistry of this adduct is summarised in Scheme 6. Hydrogenation using palladium charcoal as catalyst gave the O-succinate derivative (126), whose u.v. spectrum is virtually identical to that of the parent adduct (124).
Scheme 6.

The Chemistry of the Maleate Adduct (124).

(126) \[ \text{H}_2/\text{Pd-C} \rightarrow \]

(127) + (128) \[ \text{Me} \]

(129) \[ \text{Me} \]

(130) \[ \text{Zn}/\text{AcOH} \rightarrow \]

(131) \[ \text{Br}_2/\text{AcOH} \rightarrow \]

(132) \[ R = \text{H} \]

(133) \[ R = \text{Br} \]
The n.m.r. spectrum shows clearly the succinate protons as a one-proton triplet and a two-proton doublet at 4.81 and 7.18\(\tau\)\((J6)\) respectively.

Hydrogenation of adduct (124) using Adams' catalyst resulted in the formation of the phenol (127) by hydrogenolysis. The u.v. spectrum of this phenol appears to show the characteristic bathochromic shift in alkaline solution; the shoulder observed at 270nm in neutral solution is replaced by a band at 302nm in alkaline solution. With phenol itself the corresponding shift is from 270 to 287nm;\(^9\) the bathochromic shift of the aromatic end-absorption (from ca. 210 to 235nm for phenol\(^9\)) is obscured by the heteroaromatic absorption in the case of (127). The i.r. spectrum of compound (127) shows no phenolic O-H stretching frequency; this is to be expected, as a result of strong hydrogen-bonding to the \(\alpha\)-ester carbonyl group. Also, no trace of the phenolic proton was found in the n.m.r. spectrum despite a careful search in the range down to -30\(\tau\). The compound gave no colouration with ferric chloride solution.

An attempt to prepare a further sample of the phenol (127) from adduct (124) using fresh Adams' catalyst gave a phenol as previously; in addition however the quinoline nucleus suffered partial reduction. Variation in the activity of individual samples of Adams' catalyst is well-known.\(^9\) The n.m.r. spectrum of this product shows one aromatic methyl group; the other two methyl groups appear as doublets in the aliphatic region (8.5-9\(\tau\)). The structure
(128) most easily accommodates this data, although preferential reduction of the pyrido- rather than the benzo-ring might normally have been expected. Nevertheless, the compound (128) was methylated smoothly with ethereal diazomethane to give the ether (129), a result which gives chemical confirmation of the phenolic nature of the hydrogenolysis products (127) and (128).

Reduction of adduct (124) with zinc in glacial acetic acid gave a yellow compound shown by analysis and the mass spectrum to have a molecular weight of 441, indicating that the compound is a tetrahydro-derivative of the hydrogenolysis product (127). The n.m.r. spectrum shows three ester-methyl resonances, three singlet methyl resonances in the range 7.3-7.6\( \tau \), and a complex pattern in the region 6.3-7.4\( \tau \) integrating to three protons; there is also a one-proton doublet at 5.86\( \tau \), \( J = 5.2 \text{Hz} \), which shows signs of further splitting. These data,
together with the u.v. spectrum which shows a considerably greater degree of conjugation than that of compound (127), suggest a structure such as (130); protonation of the nitrogen atom would account for the hypsochromic shift of the u.v. spectrum which is observed in acid solution.

The doublet at 5.86\(\tau\) in the n.m.r. spectrum is assigned to the 4'- or 6'-proton; it is assumed that one of the vicinal methylene protons is only weakly coupled to this proton.\(^{81}\) No O\(\overline{H}\) proton resonance was found; an NH resonance is possibly obscured in the region 6-7.7\(\tau\). A spectrum run in the presence of D\(_2\)O was poorly resolved but appeared to show little change. No O-H stretching frequencies are visible in the infra-red spectrum above 3000cm\(^{-1}\), possibly as a result of hydrogen-bonding.

Two products, both mixtures, were isolated from the reaction of the adduct (124) with bromine in glacial acetic acid. The first, colourless product, which was shown by thin-layer chromatography to contain several components, shows no maleate-proton in the n.m.r. spectrum; this suggests the presence of the compound (131) resulting from addition of a molecule of bromine across the maleate double-bond. A singlet at 3.3\(\tau\) is assigned to the -O-CEBr.CHEBr proton.
Also, however, the ester-methyl resonances are not sharp; there is an extra peak at 6.88, integrating to rather less than two protons, and the aromatic-methyl resonances integrate to about six protons. These results suggest the presence of a compound or compounds formed by bromination of an aromatic methyl group, possibly the 4-methyl group; such attack is known to occur, e.g. in the formation of the dibromo-compound (134) by bromination of the methylazepine (59).

The mass spectrum of the colourless product shows a weak dibromo-pattern at m/e ca. 740 (average M.W. of compound
(131) is 739) and a much stronger monobromo-doublet with peaks at m/e 657 and 659.

The second product, isolated in very low yield, was yellow and appears to be a mixture of the monobromo-derivative (132) and a dibromo-derivative, possibly (133). The n.m.r. spectrum shows the presence of only three aromatic protons, and again partial bromination of an aromatic methyl-group is indicated by the peaks in the region 6.8-7.5. The mass spectrum shows strong dibromo- and monobromo-patterns. This phenolic bromination supports the substitution pattern shown in structure (127) for the 2-phenyl group, with a hydrogen atom ortho to the hydroxyl group; bromination at this 5'-position is however likely to be somewhat slower than in the case of simple phenols, because of steric crowding and the presence of four deactivating substituents.

The analogue of the hydrogenolysis product (127) was obtained on one occasion from the reaction of 2,8-dimethyl-quinoline with dimethyl acetylenedicarboxylate in tetrahydrofuran; this product is assigned the structure (135),

(132) R = H
(133) R = Br
although the isomeric structure (137) is not excluded (p. 48). This product was not isolated on any other occasion. The spectral properties parallel those of the analogue (127); the 4-proton appears in the n.m.r. spectrum as a characteristic low-field doublet in both deuteriochloroform and trifluoroacetic acid solution. Methylation with ethereal diazomethane yielded the ether (136) (possibly (138)) analogous to the product which would have been obtained had the phenol (127), rather than the tetrahydro-derivative (128), been available for methylation.

The maleate adduct (124) and the 1:1 adduct (121) do not form methiodides on treatment with methyl iodide in boiling acetonitrile (cf. p. 48). Steric hindrance of the nitrogen atom, particularly in the case of adduct (124) is a possible cause, but as previously a decrease in the nucleophilic strength of the nitrogen atom through conjugation with the 2-substituent is likely to be of importance. The isomeric 1:1 adduct (122) also does not form a methiodide under these conditions.
Scheme 7.
Mechanism for Formation of the Maleate Adduct (124).

\[
\text{Pyridine} \xrightarrow{-H^+} \text{Pyridine} \xrightarrow{\text{EC} \equiv \text{CE}} \text{Product} (139)
\]

\[
\text{Pyridine} \xrightarrow{\text{EC} \equiv \text{CE}} \text{Product} \xrightarrow{+H^+, -\text{MeOH} \text{ or } -\text{OMe}} \text{Product} (140)
\]
A reaction scheme to account for the formation of the adducts (124) and (135) is proposed (Scheme 7). The initial stages are similar to those of the mechanism of formation of the red adducts, except that no N-side-chain is involved. This scheme requires that the single proton of the 2-phenyl group be ortho to the hydroxyl group; chemical confirmation of this substitution pattern is provided by the bromination results discussed above. An alternative mechanism could operate, in which the intermediate (139) attacks a second mole of ester as in the new azepine mechanism to give (141), which then cyclises and rearranges in a similar fashion to (140), giving ultimately the alternative structural types (142) and (143). The chemistry of the maleate adduct is equally

(139) ECCE →

(141)

(141) →

(142) R = H
(143) R = maleyl
compatible with both structures, although intramolecular hydrogen-bonding of the phenolic hydrogen atom is not possible with structure (142). It does not appear possible to differentiate satisfactorily between these alternatives except by unambiguous syntheses.

Yellow adducts formed from three moles of ester and one of the heterocycle were isolated from the reactions of 2,8-dimethyl-, 2,6,8-trimethyl- and 2,4,6,8-tetramethyl-quinoline with dimethyl acetylenedicarboxylate in acetonitrile. These adducts are tentatively assigned the structures (144), (145) and (146) respectively. The adduct (144) from 2,8-dimethylquinoline was isolated only once; it was not detected when the reaction was repeated on several further occasions.

\[
\text{(144) 1-Me} \\
\text{(145) 1,3-Me}_2 \\
\text{(146) 1,3,5-Me}_3
\]
Table 8  
Observed and Calculated AMX System of Adduct (144).

<table>
<thead>
<tr>
<th>$f_{\text{obs}}$</th>
<th>$f_{\text{calc}}$</th>
<th>calc.intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>450.3</td>
<td>450.2</td>
<td>0.90</td>
</tr>
<tr>
<td>440.0</td>
<td>440.0</td>
<td>1.95</td>
</tr>
<tr>
<td>429.7</td>
<td>429.7</td>
<td>1.15</td>
</tr>
<tr>
<td>322.7</td>
<td>322.7</td>
<td>0.90</td>
</tr>
<tr>
<td>312.3</td>
<td>312.4</td>
<td>0.75</td>
</tr>
<tr>
<td>309.8</td>
<td>309.7</td>
<td>1.25</td>
</tr>
<tr>
<td>299.4</td>
<td>299.5</td>
<td>1.10</td>
</tr>
<tr>
<td>245.3</td>
<td>245.2</td>
<td>1.25</td>
</tr>
<tr>
<td>235.1</td>
<td>234.9</td>
<td>1.10</td>
</tr>
<tr>
<td>232.2</td>
<td>232.2</td>
<td>0.85</td>
</tr>
<tr>
<td>222.0</td>
<td>221.9</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Input parameters: $W_1 = 234.200$, $W_2 = 439.000$, $W_3 = 310.700$, $J_{12} = 10.200$, $J_{13} = -13.000$, $J_{23} = 10.300$

$f_{\text{obs}}$, $f_{\text{calc}}$. line positions; $W$, chemical shifts in Hz downfield from internal TMS. $J$, coupling constants in Hz. At 100MHz.
Certain structural features are suggested by the spectral data of these adducts. The n.m.r. spectra of the adducts (144) and (145) show one-proton doublets at ca. 2:1 and 3.1τ (CDCl₃ solution), while the spectrum of adduct (146) shows a broad one-proton singlet at 2.3τ. These values suggest the presence of a conjugated system, as shown, in which the 6-proton is deshielded by the peri 7-ester group; the effect is analogous to that observed with the simple azepines (Chapter 2).

The n.m.r. spectrum of adduct (144) from 2,8-dimethylquinoline shows a three-spin AMX system comprising a triplet and two double-doublets centred at 5.60, 6.90 and 7.67τ respectively; the X-branch is partially obscured by aromatic-methyl resonances in the spectra of adducts (145) and (146). This pattern indicates the presence of a -CH₂-CHX group; a 100 MHz spectrum calculated using the three-spin programme of Wilkins and Klopfenstein is in good agreement with the observed spectrum of the 2,8-dimethylquinoline adduct (144) (Table 8). The presence of a methylene group in the system is further indicated by the high value of one of the coupling constants (J₁₃=13.0 Hz; since the spectrum is first-order the negative sign, indicating that the protons are geminal, is not important in the calculation).

The u.v. spectra of these adducts are unchanged in strong acid; this resistance to protonation may be a consequence of steric hindrance, although the structures (144)-(146) might be expected to protonate at position 7.
by analogy with the simple azepines. The principal feature of the mass spectra is the occurrence of a very strong peak at $\text{m/e } M - 355$; metastable-ion peaks confirm that a fragment of mass 355 is lost from the molecular ion in all three cases. This fragment possibly has the structure (147), which would be resonance-stabilised as shown.

\[
\begin{align*}
\text{Adduct (146)} & \quad \text{[Resonance structures]} \\
& = \text{Molecule (147)}
\end{align*}
\]

Attempts to reduce the 2,4,6,8-tetramethylquinoline adduct (146) with zinc in glacial acetic acid, and catalytically using 10% palladium-on-charcoal and Adams' catalyst, were unsuccessful. Irradiation of a methanolic solution of adduct (146) with ultra-violet light however yielded a photoisomer whose u.v. spectrum is considerably less conjugated
than that of the parent adduct (146). The n.m.r. spectrum shows what appears to be a very high-field ester-methyl resonance at 7.11 ppm. The structure (146) could ring-open to give the diradical (148), which might rearrange to give the structure (149), or the structure (150) by recycylation. Such suggestions however can be regarded as being only very tentative.
As far as is possible, Parts 2, 3 and 4 refer to Chapters 2, 3 and 4 respectively. The reactions of 2,8-dimethyl- and 2,6,8-trimethyl-quinoline with dimethyl acetylenedicarboxylate are described in Part 3, and that of 2,4,6,8-tetramethylquinoline with the ester is described in Part 4.
PART ONE

INSTRUMENTS AND GENERAL PROCEDURES.

Infra-red absorption spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer and unless otherwise stated are for Nujol mulls. Wavenumbers of absorptions are quoted in cm$^{-1}$; br = broad, infl. = point of inflexion, w = weak.

Ultra violet absorption spectra were recorded on a Perkin-Elmer Model "137-UV" spectrophotometer fitted with a deuterium lamp, in methanolic solution using 1 cm. silica cells. The solvent methanol was first dried by boiling under reflux with magnesium turnings and was then carefully distilled. Spectra were recorded as necessary in methanol (M), methanol acidified with three drops of 72\% aqueous perchloric acid (MA), methanol basified with three drops of 2N sodium hydroxide solution (MB), MeOH-0.2N NaOH soln. (1:1 v/v) (B) and MeOH-72\% perchloric acid (2:1 v/v) (P). Absorption maxima are quoted in nm with 10$^{-4}$ C in parentheses.

N.M.R. spectra were recorded at 60MHz on either a Perkin-Elmer R10 or an R12 n.m.r. spectrometer, and at 100 MHz on a Perkin-Elmer R14 n.m.r. spectrometer; the operating temperature was 34°, and tetramethylsilane was used as internal standard. Chemical shifts are quoted as $\tau$-values and coupling constants in Hz.
Mass spectra were recorded on either an A.E.I. MS9 high-resolution mass spectrometer or a Varian CH7 mass spectrometer; both instruments were fitted with direct insertion probes and were operated at an ionisation voltage of 70 eV. Peak heights, expressed as percentages of the height of the base peak, are quoted in parentheses. \( m^* \) = metastable-ion peak.

Irradiations were carried out with a Hanovia 450w mercury-vapour lamp surrounded by a water-cooled quartz thimble which was placed in the reaction vessel. Compounds were irradiated under nitrogen.

Melting-points were recorded on a Reichert Microscope "RCH" Kofler Micro-heating stage and are uncorrected.

Evaporation of organic solvents was carried out with a Büchi Rotavapor-R, using a water-bath of temperature 40-50°.

Thin Layer Chromatography (t.l.c.) was performed using (i) coated 20 x 5 cm. glass plates prepared as follows. Kieselgel PF_{254} (E.Merck AG) (30g.) was slurried with distilled water (70ml.) for 2 min. and then spread to a thickness of 30μ using Shandon apparatus. The plates were allowed to set and were then dried at 105° for 40 min.

(ii) precoated plastic sheets, "Polygram SIL N-UV\textsubscript{254}"
(Macherey-Nagel and Co., Dürren).

4:1 v/v Toluene: ethyl acetate was used as eluant.

Preparative Thin Layer Chromatography was performed on 1m. x 20cm. plates. Kieselgel PF\textsubscript{254} (80g.) was slurried with distilled water (200ml.) for 2 min. and spread to a
thickness of 1mm. using Shandon apparatus. The plates were dried at 40° for 5hr. in a Shandon oven.

Alumina for Column Chromatography was Spence grade H, 100/200s mesh, deactivated by shaking with 5% by volume of 10% aqueous acetic acid and standing overnight before use. Columns were made up in petrol (b.p. 60-80°) or benzene unless otherwise stated. "Petroleum columns" were eluted successively with light petroleum (b.p. 60-80°), light petroleum-benzene mixtures containing increasing proportions of benzene, benzene and benzene-chloroform mixtures containing increasing proportions of chloroform. Similarly, benzene columns were eluted with benzene and benzene-chloroform mixtures. These procedures are referred to in the following pages as "chromatography on alumina".

Microanalyses were by Dr. G. Weiler and Dr. F. B. Strauss, Oxford. Light petroleum had b.p. 60-80° unless otherwise stated. The acetonitrile used as a reaction solvent was dried over phosphorus pentoxide and distilled before use. All liquid reagents were also distilled immediately before use. Unless otherwise stated, dried magnesium sulphate was used to dry ether and chloroform solutions.

PREPARATION AND PURIFICATION OF REAGENTS

Dimethyl acetylenedicarboxylate was supplied by Koch-Light Laboratories Ltd. and re-distilled before use; b.p. 94-96°/15mm. Hg.
Diethyl acetylenedicarboxylate: a sample prepared from the monopotassium salt of acetylenedicarboxylic acid by a literature method was available; b.p.116-118°/17 mm.

Both the dimethyl and the diethyl esters were stored at ca. 0° to minimise polymerisation.

2-Methylquinolines.

2-Methylquinoline (quinaldine) was supplied by B.D.H. Chemicals Ltd. and re-distilled; b.p.118-121°/15 mm.

2,3-Dimethylquinoline and 2-Ethylquinoline.

A crude mixture of 2,3-dimethylquinoline and 2-ethylquinoline was prepared by a Pfitzinger synthesis starting from isatin and methyl ethyl ketone, using the procedure of Plant and Rosser. The crude mixture of quinolines (50g.) in boiling ethanol was added with stirring to a boiling solution of picric acid (70g.) in ethanol (700ml.), boiling maintained for 10 min. and the mixture filtered hot. 2,3-Dimethylquinoline picrate, yellow prisms, m.p.228-230° (lit.229°) was filtered off. The filtrate on cooling rapidly deposited 2-ethylquinoline picrate; recrystallisation from ethanol gave yellow plates (19g.), m.p.148° (lit.148°). Decomposition of the picrates with hot dilute ammonia solution yielded respectively 2,3-dimethylquinoline (13g.), m.p.67° (lit.68-69°) (from light petroleum, b.p.40-60°) and 2-ethylquinoline (6.0g.), b.p.136-139°/20 mm.
2-Ethylquinoline was obtained more easily by Doebner's procedure. A solution of propionaldehyde (110 ml.) and pyruvic acid (100 ml.) in ethanol (500 ml.) was added slowly to a solution of aniline (140 ml.) in ethanol (500 ml.). The mixture was heated under reflux on a boiling-water bath for 5 hr., evaporated to a volume of 1 l. and cooled to 0°. The precipitate of 2-ethylquinoline-4-carboxylic acid was collected, washed with petrol and water and thoroughly dried (35 g., 12%). The powdered acid was then decarboxylated by dry distillation, yielding 2-ethylquinoline (8.2 g., 3.6% based on pyruvic acid).

2,4-Dimethylquinoline was prepared from aniline and acetylacetone by the method of Combes; b.p. 138-140°/20 mm.

2,8-Dimethylquinoline.

(i) (after Bowen et al.) To a 1-litre, 3-necked flask equipped with sealed stirrer, 250 ml. dropping funnel, thermometer and air condenser were added in order water (100 ml.), "sulfomix" (404 g.) (containing 0.6 mole m-nitrobenzenesulphonic acid) (kindly supplied by Dr. W.R. Tully) and o-toluidine (107 ml.). The mixture was heated on an oil bath to 105° and crotonaldehyde (138 ml.) was added dropwise with vigorous stirring over 35 min., the temperature being maintained in the range 105-110°. The temperature was then raised to 125° over 20 min. with very vigorous stirring to prevent loss through foaming. The mixture was then poured before it could stiffen on to crushed ice (1.5 Kg.) in a 5 l. beaker, basified with
sodium hydroxide solution and steam-distilled until
10 l. distillate had collected. The distillate was
extracted with chloroform (3x500 ml.) and the combined
chloroform extracts were washed, dried and evaporated.
The residue was distilled in vacuo, three fractions being
taken: (i) 98-108°/4 cm. (40 ml.) (unreacted o-toluidine);
(ii) 108-130°/4 cm. (15 ml.) (mixture of o-toluidine and
2,8-dimethylquinoline); and (iii) 130-138°/4 cm. (crude
2,8-dimethylquinoline). The crude product (fraction (iii),
weight 27.5 g.) was purified via the picrate, giving pure
2,8-dimethylquinoline (9.9 g., 6.3%), b.p. 136-137°/30 mm.
(lit. 93-95°/2 mm.).

(ii) To a 2 l. 3-necked flask fitted with a mechanical
stirrer, reflux condenser and dropping funnel were added
o-toluidine (214 ml.), powdered arsenic pentoxide (32 g.)
and concentrated hydrochloric acid (460 ml.). The mixture
was heated to ca. 100° on a boiling-water bath with stirring
and crotonaldehyde (179 ml.) was added carefully over 15 min.;
vigorous reaction ensued. Stirring was continued at
ca. 100° for 3 hr.; the solution was then cooled to 0° and
the excess of o-toluidine diazotised by addition of ice-
cold sodium nitrite solution. After warming to 60° for
1 hr. to convert the diazonium salt to the phenol, the
solution was basified with sodium hydroxide solution and
extracted with ether (4x500 ml.), and the combined ether
extracts were washed, dried and evaporated. The residue
was distilled in vacuo, giving crude 2,8-dimethylquinoline
as a yellow liquid (103 g.), b.p. 142-155°/25 mm.
The crude product (40g.) in light petroleum (b.p. 40-60°) (100 ml.) was chromatographed on alumina (1250 ml. in petrol). Elution of a thin, pale yellow band with petrol gave, after evaporation and distillation of the residue in vacuo, a colourless product (10g.), b.p.132-134°/20 mm., shown by the n.m.r spectrum to be a mixture of 2,8-dimethylquinoline and unreacted o-toluidine. Subsequent elution with petrol of the main, pale yellow band gave after evaporation and distillation pure 2,8-dimethylquinoline (21.5g.), b.p.132-134°/20 mm.

The remainder of the crude 2,8-dimethylquinoline (63g.) was chromatographed similarly on alumina (1800 ml.), yielding 19.2g. pure product. Overall yield of 2,8-dimethylquinoline, 40.7g. (13%).

Method (ii) was much more convenient and satisfactory.

2,6,8-Trimethylquinoline.

An impure sample prepared by S.H. Purshouse from 2,4-xylidine and crotonaldehyde using the procedure of method (ii) for 2,8-dimethylquinoline (above) was available. The n.m.r. spectrum showed the presence of reduced reaction intermediates.

The crude quinoline (97g.) was added cautiously to a solution of chromium trioxide (68g.) in water (1200 ml.). The orange chromate was collected, washed thoroughly with cold water and recrystallised from water. Decomposition of the purified chromate with 4N sodium hydroxide soln. (800 ml.) yielded pure 2,6,8-trimethylquinoline (13g.), b.p.156-158°/30 mm., which solidified on standing at 0°.
A further sample of crude 2,6,8-trimethylquinoline was recrystallised from ethanol; m.p. 46° (lit. 104° 46°).

2,4,6,8-Tetramethylquinoline was prepared from 2,4-xylidine and acetylacetone by the method of Combes; m.p. 85° (lit. 86°) (from petrol).

4-Chloro-2-methylquinoline.

2-Methylquinolin-4-one (32g.), prepared as described and thoroughly dried, was added portionwise to freshly-distilled phosphorus oxychloride (80 ml.). The mixture was heated under reflux on a boiling-water bath for 2 hr. and poured while hot on to a mixture of ice (500g.) and water (500 ml.) with stirring. The resulting deep red solution was made strongly alkaline with sodium hydroxide solution and extracted with ether (3x500 ml., 1x250 ml.). The combined ether extracts were dried and evaporated and the dark residue distilled in vacuo, giving 4-chloro-2-methylquinoline (27g., 75%), b.p. 142-143°/20 mm. (lit. 269-270°/a.p. for the product of another procedure), n.m.r.: ArH(4) and 3-H, 1.8-2.57 m; 2-Me, 7.32 (CDCl₃ soln.).

2-Isopropylquinoline.

A solution of aniline (120 ml.) in ethanol (700 ml.) was added slowly to a solution of pyruvic acid (95 ml.) and isobutyraldehyde (139 ml.) in ethanol (750 ml.). The mixture was heated under reflux on a boiling-water bath for 5 hr. and allowed to cool; a white solid separated and was collected (7.0g., m.p. 212°). The filtrate was treated with water (100 ml.) and allowed to stand for several hours.
A pale brown precipitate was collected and washed with ethanol; the mother-liquor later deposited a fairly pure sample of 2-isopropylquinoline-4-carboxylic acid (2.9g.), m.p.140°.

The pale brown solid was dissolved in 2N sodium hydroxide solution (2 l.) with warming, a small amount of insoluble residue was removed by filtration, and the filtrate was acidified with glacial acetic acid, giving a precipitate of 2-isopropylquinoline-4-carboxylic acid (19.6g.), m.p.148° (lit.148°146°). Total yield of acid, 22.5g. (8.9%). On another occasion a sufficiently pure sample of the acid (12.8g.) was obtained without the purification via the sodium salt.

The combined samples of the acid (35.3g.) were powdered and dry distilled, giving 2-isopropylquinoline (9.7g.), b.p.124-126°/15 mm. (lit.1825°/a.p.).

An attempt to prepare 2-isopropylquinoline-4-carboxylic acid by a Pfitzinger synthesis from isatin and methyl isopropyl ketone was unsuccessful.

**PART TWO**

Reaction of 2,3-Dimethylquinoline with Dimethyl Acetylene-dicarboxylate.

2,3-Dimethylquinoline (5.0g.) in acetonitrile (30 ml.) was added slowly with swirling to the ester (12 ml.) in acetonitrile (70 ml.) at 0° and the mixture kept at 0° for 24 hr. After 18 days at room temperature the dark crystals
which had formed were collected, washed with acetonitrile
and methanol, and the filtrate and washings combined,
evaporated and retained (A). The crystals (1.96g.) in
the minimum of chloroform were chromatographed on alumina
(150 ml. in benzene). Elution of an orange band gave
tetramethyl 10,11-dihydro-6-methylazepino[1,2-a]quinoline-
7,8,9,10-tetracarboxylate (58) (1.68g.), red-orange prisms
(from methanol-acetonitrile), m.p.200-201°C (Found:
C, 62.7; H, 5.3; N, 3.4. C_{23}H_{23}NO_8 requires C, 62.6; H,
5.3; N, 3.2%). ν_max. 1736, 1722inf1, 1718, 1688inf1, 1685,
1619, 1542inf1, 1539, 1490, 1450, 1434 cm.^{-1}.

A, in the minimum of chloroform, was chromatographed
on alumina (400 ml. in benzene). An orange-red band was
eluted, but since separation of the constituents was not
effected the combined eluates were evaporated and the
residue in benzene was re-chromatographed on activated
alumina (200 ml. in benzene). Elution of a yellow-orange
band yielded mixed orange-yellow crystals (7.2g.), from
which were isolated by careful fractional crystallisation
from methanol and methanol-acetonitrile three compounds
(decreasing order of solubility): (i) tetramethyl 4a,5-
dimethyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate
(52) (1.62g.), pale yellow prisms (from methanol), m.p.
116-118°C (Found: C, 63.0; H, 5.3; N, 3.1. C_{23}H_{23}NO_8 requires
C, 62.6; H, 5.3; N, 3.2%). ν_max. 1754, 1736, 1727, 1713,
1622, 1539, 1484, 1437 cm.^{-1}; (ii) tetramethyl 10,11-
dihydro-6-methylazepino[1,2-a]quinoline-7,8,9,11-tetra-
carboxylate (64) (0.11g.), orange prisms (from methanol),
Further elution of a dark red-brown band gave a dark tar (2.0g.) which was further separated on two thin-layer plates with 4:1 toluene:ethyl acetate as eluant (3 elutions). Extraction of the main, violet band followed by recrystallisation from methanol (3 times) gave a very dark green compound (40 mg.) (p. 27) as matted needles, m.p. 167.5-169° (Found: C, 59.7; H, 5.0; N, 2.4%). ν_max. 1732, 1620w, 1530br, 1477w, 1456, 1433 cm.⁻¹ (CHCl₃ soln.), λ_max. (M) 252 (4.84), 546 br (2.26); (MA) 248 (6.44), 330 (2.22); (B) 237 (7.74), 252br 1 (4.89), 293 (1.38), 298 (1.30), 309 (1.28), 322 (1.20); n.m.r.: ArH(5), 2.65-3.1 m; ester-CH₃, 6.23(6), 6.28(6), 6.35, 6.49; 3-spin AMX system 6.0-6.3 (obscured), 6.75, 7.14 (both 4 lines; J's 9-13Hz), Ar-Me, 7.96; m/e 583 (M⁺, 22%), 552(11), 524(19), 497(100), 464(39), 406(24), 378(18), 320(19), 203(11) (other peaks <7%), m* 522br (583+552,551), 462(524+492), 437(492+464), 423.5(583+497), 402.3(464+432), 376.5(438+406), 344.5(406+374).

Reaction of 2,4-Dimethylquinoline with Dimethyl Acetylene-carboxylate.

2,4-Dimethylquinoline (10g.) in acetonitrile (50 ml.) was added slowly with swirling to the ester (23 ml.) in acetonitrile (150 ml.) at 0° and the mixture kept at 0° for 24 hr. After 12 days at room temperature the acetonitrile
was evaporated and the resulting tar in benzene-chloroform was chromatographed on alumina (750 ml. in petrol).

Elution of a yellow-red band yielded tetramethyl 4a,6-dimethyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (53) (5.7g.), matt-yellow rods (from methanol), m.p.124-126° (Found: C, 62.6; H, 5.4; N, 3.2. \( \text{C}_{23}\text{H}_{23}\text{NO}_8 \) requires C, 62.6; H, 5.3; N, 3.2%). \( \nu_{\text{max}} \) 1742, 1737, 1732, 1704, 1643w, 1627, 1570w, 1540, 1481, 1452, 1434br cm.\(^{-1}\).

Further elution of a slightly redder band yielded the azepine (59) (3.6g.), m.p.218-219.5° (lit. \(^{45} \) 217-218°) and a further crop of the quinolizine (53) (0.9g.).

**Reaction of 4-Chloro-2-Methylquinoline with Dimethyl Acetylenedicarboxylate.**

4-Chloro-2-methylquinoline (10g.) in acetonitrile (50 ml.) was added slowly with swirling to the ester (21 ml.) in acetonitrile (150 ml.) at 0° and the mixture kept at 0° for 24hr. After 3 weeks the acetonitrile was evaporated and the resulting tar in benzene was chromatographed on alumina (700 ml. in petrol). Elution of a yellow band yielded tetramethyl 6-chloro-4a-methyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (55) (1.83g.), brilliant yellow needles (from methanol), m.p.126-128° (Found: C, 57.0; H, 4.3; N, 2.9; Cl, 7.2. \( \text{C}_{22}\text{H}_{20}\text{NO}_8\text{Cl} \) requires C, 57.2; H, 4.4; N, 3.0; Cl, 7.7%). \( \nu_{\text{max}} \) 1738, 1723, 1716, 1706, 1700, 1610, 1600, 1571w, 1510, 1479, 1454, 1433, 1411 cm.\(^{-1}\).

Further elution of a deep orange band yielded a semi-
-solid tar which on trituration with methanol gave a solid; this was recrystallised twice from methanol-acetonitrile to give tetramethyl 5-chloro-10,11-dihydro-azepino[1,2-a]quinoline-7,8,9,10-tetracarboxylate (61) (3.3g.) as orange prisms, m.p.176-178° (Found: C, 57.1; H, 4.3; N, 3.0; Cl, 7.5. C_{22}H_{20}NO_{8}Cl requires C, 57.2; H, 4.4; N, 3.0; Cl, 7.7%), ν_{max}. 1745br, 1678br, 1609br, 1560, 1547, 1485, 1450, 1436 cm^{-1}. The mother liquor from the recrystallisations yielded a further crop of the quinolizine (55) (0.5g.).

Hydrolysis of the Azepine (61).

(i) The azepine (61) (0.5g.) was heated under reflux in saturated methanolic hydrogen chloride containing two drops of distilled water for 30 min. The colourless solution was evaporated to give a yellow tar which was dissolved in a small amount of methanol. Addition of water gave an oil which rapidly crystallised. The yellow crystals were collected and recrystallised from methanol to give tetramethyl 10,11-dihydro-5-methoxyazepino[1,2-a]quinoline-7,8,9,10-tetracarboxylate (63) (0.35g.) as yellow parallelepipeds, m.p.197-199° (Found: C, 60.2; H, 5.1; N, 3.1. C_{23}H_{23}NO_{9} requires C, 60.4; H, 5.1; N, 3.1%), ν_{max}. 1763, 1730, 1698, 1688, 1679, 1634, 1630, 1573, 1563, 1502, 1447, 1412 cm^{-1}.

(ii) The azepine (61) (0.5g.) was heated under reflux with a mixture of methanol (20 ml.), water (4 ml.) and concentrated hydrochloric acid (6 ml.) for 1½ hr. The
yellow solution was evaporated to give a tar which was
dissolved in methanol. Addition of water gave an oil
which on cooling and scratching gave a yellow, crystalline
mixture (110 mg.), n.m.r.: 1.60d(J7); ArH, 2.1-3.1 m;
3.8s; ester-Me, 6.0-6.9 m; CH-CH₂, 6.0-7.5 m (p. 21).

Reaction of 2-Methyl-3-Phenylquinoline with Dimethyl
Acetylenedicarboxylate.

2-Methyl-3-phenylquinoline (kindly supplied by
J.K.Stubbs) (10g.) in acetonitrile (10,ml.) was added
slowly with swirling to the ester (17 ml.) in acetonitrile
(100 ml.) at room temperature. After 11 days at room
temperature the acetonitrile was evaporated and the
resulting tar in benzene was chromatographed on alumina
(750 ml. in petrol). First eluates yielded dimethyl
fumarate (120 mg.). Elution of an orange-red band yielded
tetramethyl 10,11-dihydro-6-phenylazepino[1,2-a]quinoline-
7,8,9,10-tetracarboxylate (62) (7.0g.), red prisms (from
methanol-acetonitrile), m.p.196-198° (Found: C, 67.0;
H, 5.2; N, 3.0. C₂₈H₂₅NO₈ requires C, 66.8; H, 5.0; N, 2.8%),
υₘₐₓ. 1764, 1748, 1732, 1699, 1695, 1616, 1569, 1562,
1470 cm⁻¹.

The mother liquors from the recrystallisation of the
azepine (62) were evaporated and re-chromatographed on
alumina (900 ml.in 1:1 petrol:benzene). Elution of a
pale yellow band yielded a yellow compound (5 mg.), fine
rods (from methanol), m.p.213-215°, λₘₐₓ. (M) 287(1.33),
344(1.07), 422inCl(2.18), 454(2.29) (no change in MA),
m/e 471(9%), 412(100), 265(3), m* 360.5 (471+412).

An M.W. of 471 corresponds to composition 1 mole base + 2 moles ester-MeOH.

Further elution of a bright yellow band yielded tetrabutyl 4a-methyl-5-phenyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (56) (3.1g.), yellow parallelepipsds (from methanol), m.p.130-131.5° (Found: C, 66.8; H, 5.0; N, 2.8. C_{28}H_{25}NO_{8} requires C, 66.8%; H, 5.0; N, 2.8%), v_{max.} 1747, 1720, 1707, 1606, 1520, 1497, 1441, 1418 cm.^{-1}. Continued elution of an orange-yellow band yielded azepine (62) (260 mg.).

Reaction of 2-Ethylquinoline with Dimethyl Acetylene-dicarboxylate.

2-Ethylquinoline (8.2g.) in acetonitrile (10 ml.) was added slowly with swirling to the ester (19 ml.) in acetonitrile (200 ml.). After 48hr. at room temperature the acetonitrile was evaporated and the resulting tar in benzene-chloroform was chromatographed on alumina (900 ml. in benzene). Elution of an orange band yielded a tar which on trituration with methanol deposited crystals of tetrabutyl 10,11-dihydro-11-methylazepino-[1,2-a]quinoline-7,8,9,10-tetracarboxylate (68) (8.2g.), orange rods (from acetonitrile), m.p.193° (Found: C, 62.8; H, 5.2; N, 3.4. C_{23}H_{23}NO_{8} requires C, 62.6; H, 5.3; N, 3.2%), v_{max.} 1752, 1729, 1674, 1619, 1562, 1556, 1490, 1452, 1438, 1412 cm.^{-1}.

After elution the column was run dry and extruded, and a blue band was collected and extracted with acetone-
-chloroform. The solvent was evaporated, leaving a dark solid which on recrystallisation from methanol (twice) gave the 2-ethylquinoline blue adduct (Part Two) (15 mg.), m.p. 242-246° (turning green), \( v_{\text{max}} \) 1733 br, 1619, 1604, 1561 w, 1534, 1452, 1432, 1418 cm\(^{-1}\) (CHCl\(_3\) soln.).

The mother liquors from the crude azepine (68) were evaporated and re-chromatographed on alumina (400 ml. in benzene). Elution of an orange band gave tetramethyl 10,11-dihydro-10-methylazepino[1,2-a]quinoline-7,8,9,11-tetracarboxylate (71) (0.12 g), orange parallelepipeds (from methanol-acetonitrile), m.p. 170-171.5° (Found: C, 62.8; H, 5.3; N, 3.2. \( C_{23}H_{23}NO_8 \) requires C, 62.6; H, 5.3; N, 3.2%), \( v_{\text{max}} \) 1758, 1750, 1738, 1660, 1629, 1618, 1573, 1496, 1448, 1421 cm\(^{-1}\).

**Attempted Oxidation of the Azepine (68) with Chromic Acid.**

Sodium dichromate (8.2 g.) in warm glacial acetic acid (25 ml.) was added in portions to the azepine (68) (8.2 g.) in boiling glacial acetic acid (50 ml.), and boiling was continued for 8 min. Methanol was added to destroy unused oxidant, and the solvent was evaporated. This last process was repeated, and the resulting dark green tar was dissolved in water (150 ml.). The solution was extracted with chloroform (1x100 ml., 2x50 ml.), and the combined chloroform extracts were washed with water, dried and evaporated. The resulting tar in benzene was chromatographed on alumina (500 ml. in benzene). The material gave at first a deep red band on the column, but
this turned yellow as the column was eluted with benzene-chloroform. This yellow band was eluted and yielded a dark tar (0.21g.) which could not be induced to crystallise, \( \lambda_{\text{max}} \) (M) (optical densities in parentheses) 233(0.48), 304(0.068), 317(0.055); (P) 244(0.65), 322(0.18); \( \text{n.m.r.} \): (very poorly resolved) ArH, 1.7-3.1 m; ester-Me, 6.1-6.5 m; aliphatic protons, 6.86s, 8.4-9.3 m (integration not accurate).

**Reaction of 2-Ethylquinoline with Diethyl Acetylenedicarboxylate.**

2-Ethylquinoline (2.0g.) in acetonitrile (25 ml.) was added slowly with swirling to the ester (5.4 ml.) in acetonitrile (50 ml.) at 0°C and the mixture kept at 0°C for 24hr. After 4 days at room temperature the acetonitrile was evaporated and the resulting tar in benzene was chromatographed on alumina (250 ml. in benzene). Elution of an orange band gave a tar which was re-chromatographed on activated alumina (150 ml. in benzene); elution of an orange band yielded a tar which crystallised on trituration with methanol. Recrystallisation from ethanol gave tetraethyl 10,11-dihydro-11-methylazepino[1,2-a]quinoline-7,8,9,10-tetracarboxylate (69), orange-yellow needles (0.45g.), m.p. 153-154°C (Found: C, 64.8; H, 6.5; N, 2.7. \( C_{27}H_{31}NO_8 \) requires C, 65.2; H, 6.3; N, 2.8%), \( \nu_{\text{max.}} \) 1753, 1709, 1677, 1621, 1567, 1561, 1458, 1417w cm\(^{-1} \).
Reaction of 2-Isopropylquinoline with Dimethyl Acetylene-dicarboxylate.

2-Isopropylquinoline (2.0g.) in acetonitrile (15 ml.) was added with swirling to the ester (4.3 ml.) in acetonitrile (50 ml.) at room temperature. After 1 week at room temperature the acetonitrile was evaporated and the resulting tar in benzene was chromatographed on alumina (250 ml. in benzene). Elution of a yellow-orange band gave a thick oil which could not be crystallised; accordingly the oil in benzene was re-chromatographed on alumina (200 ml. in petrol). Elution of a yellow-orange band gave tetramethyl 4a-isopropyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (85) (2.7g.) as a thick oil which could not be induced to crystallise even at acetone-dry ice temperatures (Found: C, 62.2; H, 5.8; N, 2.7. C_{24}H_{25}NO_{8} requires C, 63.3; H, 5.5; N, 3.1%). \( \nu_{\text{max.}} 1737, 1608\text{w}, 1527, 1500, 1462, 1442 \text{ cm}^{-1} \) (CHCl_{3} soln.).

Photochemical Isomerisation of the Benzo[c]quinolizine (85).

The benzo[c]quinolizine (85) (1.0g.) in methanol (600 ml.) was irradiated for 2 hr. The methanol was evaporated and the residue dissolved in benzene (40 ml.); the solution was filtered and the filtrate applied to an alumina chromatography column (150 ml. in petrol). First eluates gave a trace of a white solid, possibly an indolizine.\(^{11}\) Elution of the main yellow band gave an oil which solidified on addition of ether; the solid was
recrystallised with difficulty from methanol-ether to give tetramethyl 1-isopropyl-1H-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (86) (0.2g.) as thick, yellow rods, m.p. 160-162° (Found: C, 63.3; H, 5.5; N, 3.0. C₂₄H₂₅NO₈ requires C, 63.3; H, 5.5; N, 3.1%), v max. 1770, 1739, 1697, 1640, 1627, 1615, 1570, 1546, 1443, 1413 cm⁻¹.

Further elution of a thin, red band yielded red crystals (20 mg.), shown by t.l.c. to be a mixture of an orange (slower-moving) and a yellow component.

PART THREE

Reaction of 2-Methylquinoline with Dimethyl Acetylene-dicarboxylate in Methanol.

2-Methylquinoline (20 ml.) in dry methanol (20 ml.) was added with swirling to the ester (52 ml.) in dry methanol (230 ml.) at 0°. The solution darkened rapidly and began to deposit dark crystals after ca. 1 hr. After 24 hr. at 0° and a further 48 hr. at room temperature the dark crystals were collected and washed with methanol, and the filtrate and washings were combined, evaporated and retained (A).

The crystals (30g., damp) were dissolved in chloroform (100 ml.) with heating and the solution applied to an alumina chromatography column (1300 ml. in benzene). First eluates contained unreacted ester and yielded dimethyl fumarate. Elution of the main red band gave a thick tar which crystallised on trituration with methanol.
The crude solid was recrystallised with difficulty from methanol-acetonitrile to give the first red adduct, hexamethyl 11,12,13,17-tetrahydro-9-azacyclopent[a]
phenanthrene-11,12,13,15,16,17-hexacarboxylate (38a) (2.0g.) as red prisms, m.p.241° (lit. 236°) (Found: C, 59.3; H, 4.9; N, 2.6. Calc. for C_{28}H_{27}NO_{12}: C, 59.1; H, 4.8; N, 2.5%), ν_{max} 1749, 1731, 1702, 1618, 1550, 1535, 1484, 1420 cm^{-1}.

Further elution of a blue band yielded the 2-methylquinoline blue adduct (Part Two) (0.40g.), blue rods (from methanol-acetonitrile), m.p.252° (lit. 252°) (Found: C, 58.6; H, 4.5; N, 2.0. Calc. for C_{33}H_{29}NO_{15}: C, 58.3; H, 4.3; N, 2.1; and for C_{34}H_{31}NO_{15}: C, 58.9; H, 4.5; N, 2.0%), ν_{max} 1737, 1719, 1700, 1600, 1537, 1437, 1419 cm^{-1}.

A in chloroform was chromatographed on alumina (1800 ml. in benzene). Elution of the main red band yielded a mixture of the first and second red adducts (88a,b) (2.0g.); the integral of the n.m.r. spectrum indicated that the proportion of first: second was ca.3:1. These proportions were only slightly altered after repeated attempts at fractional crystallisation.

Further elution yielded the 2-methylquinoline blue adduct (0.4g.).

This reaction was repeated on several occasions to provide the quantities of the first red adduct required for the following experiments.
Reaction of the 2-Methylquinoline First Red Adduct (88a) with Bromine in Acetic Acid.

The red adduct (88a) (2.0g.) in boiling glacial acetic acid (30 ml.) was treated dropwise with bromine (0.8 ml.) in glacial acetic acid (5 ml.) and boiling continued for 5 min. The acetic acid was evaporated, the residue was treated with benzene and the benzene was evaporated. This last process was repeated twice to remove traces of acetic acid, and the tarry residue in benzene: chloroform was chromatographed on alumina (200 ml. in benzene).

Elution of a faint yellow band yielded a compound (5 mg.), fine rods (from methanol), m.p.208-211°. The mother liquors slowly deposited large, off-white crystals which were recrystallised from hexane to give dimethyl fumarate (6 mg.), m.p.97-100° with sublimation (lit. 111 102°, sublimes). The i.r. spectrum was identical to that of an authentic specimen.

Further elution of a pale yellow band yielded 4-bromo-2-(2,3,4,5-tetramethoxycarbonylcyclopenta-1,3-dien-1-y1)quinoline (96) (0.50 g.), yellow rods (from methanol), m.p.186-188° (Found: C, 52.2; H, 3.8; Br, 15.5; N, 2.8. C22H18BrNO8 requires C, 52.4; H, 3.6; Br, 15.8; N, 2.8%), νmax. 1747, 1730, 1648w, 1611w, 1550w, 1510 cm⁻¹.

Further elution of a red band yielded unreacted red adduct (100 mg.).

The quinoline (96) did not form a methiodide on treatment with methyl iodide in boiling acetonitrile.
Debromination of the Bromo-Compound (96).

The bromo-compound (96) (0.40 g.) in methanol (100 ml.) was shaken under hydrogen (2 atm.) with 10% palladium-on-charcoal (0.2 g.) for 5 hr. Filtration and evaporation gave a yellow solid which was recrystallised from methanol to give 2-(2,3,4,5-tetramethoxycarbonylcyclopenta-1,3-dien-1-yl)quinoline (97) (0.18 g.), fine yellow rods, m.p. 138-140° (Found: C, 62.1; H, 4.4; N, 3.1. C_{22}H_{19}N_{8}O_{8} requires C, 62.1; H, 4.5; N, 3.3%), \( \nu_{\text{max}} \) (Nj) 1721 br, 1630 br, 1562 w, 1551 w, 1511, 1453, 1400 w; (CHCl₃ soln.) 1721, 1638 w, 1611 w, 1559 w, 1508, 1452, 1436 cm⁻¹.

This quinoline also did not form a methiodide on treatment with methyl iodide in boiling acetonitrile.

Reaction of a Mixture of the 2-Methylquinoline Red Adducts with Bromine in Acetic Acid.

A mixture of the red adducts (5.0 g.) (first:second ca. 3:1) in boiling glacial acetic acid (100 ml.) was treated with bromine (2 ml.) in glacial acetic acid (20 ml.) using the procedure of the above bromination experiment. The crude, tarry product in chloroform was chromatographed on alumina (350 ml. in benzene). Elution of a yellow band yielded polymeric ester (150 mg.), m.p. 170-172° (n.m.r.: one very broad peak, 6.3τ (CDCl₃ soln.), ester-Me). Further elution of a deeper yellow band yielded a solid which was recrystallised from methanol to give orange crystals (0.2 g.), m.p. ca. 90°. T.l.c. showed the presence
of two components, the faster-moving of which had an \( R_f \) value equal to that of the bromo-product (36).

Further elution of a red band yielded red crystals (150 mg.) (from methanol), m.p. ca. 230\(^\circ\), shown from the n.m.r. spectrum to be a fairly pure sample of the second red adduct (88b).

Reactivity of the 2-Methylquinoline First Red Adduct with Zinc in Acetic Acid.

Zinc dust (2g.) was added in portions to a stirred solution of the first red adduct (88a) (1.9g.) in glacial acetic acid (50 ml.) and stirring continued for 1 hr. The solution was filtered, the yellow filtrate was diluted with water (100 ml.) and extracted with chloroform (2x50 ml.), and the combined chloroform extracts were washed, dried and evaporated. The residue was treated with benzene and the solvent evaporated; this process was repeated three times to remove acetic acid, and the residue in benzene was chromatographed on alumina (120 ml. in benzene). Elution of a pale yellow band gave a yellow solid which was recrystallised from methanol, giving a mixture (0.16g.) of yellow and white crystals. A few yellow and white crystals were hand-separated, and the rest of the mixture was dissolved in methanol (5 ml.). Seeding of this solution with a yellow crystal gave a fairly pure crop of the "des-bromo"-quinoline (97) (30 mg.), m.p.133.5-136\(^\circ\), with n.m.r., i.r., u.v. and mass spectra identical to those of the product of the
above debromination reaction. A mixture of the two products melted at 130°. Concentration of the mother-liquors gave a crop of colourless crystals; these were shown by t.l.c. to be a mixture of several components and were not investigated further.

Further elution of a deeper yellow band yielded a pale yellow solid (20 mg.) which was shown by t.l.c. to contain several components; n.m.r.: ArH, 2.7-3.5 m, 3.73d (J ca.8); one(?)H, 5.14d(J8); ester CH₃(18?), 6.1-6.8; aliphatic protons, 5.9-7.8τ d (poorly resolved). This suggests the presence of an intact but reduced red-adduct structure.

Reaction of the Quinoline (97) with Diazomethane.

A sample of the des-bromo-quinoline (97) was prepared from the 2-methylquinoline first red adduct via the bromoquinoline (96) as described above. The quinoline (97) (100 mg.) in ether (100 ml.) was treated with ethereal diazomethane (generated as described from N-methyl-N-nitrosourea (3g.)), and the solution was set aside for 10 hr. Glacial acetic acid was added to decompose unreacted diazomethane and the almost colourless solution was evaporated. The residue was dissolved in methanol and the solution filtered to remove a small amount of white solid. The filtrate was evaporated, acetic acid was removed by repeated addition and evaporation of methanol, and the residue in methanol was allowed to stand overnight
at 0°. A crop of pale yellow crystals was collected and recrystallised from methanol, giving a pyrazoline (p. 46) (42 mg.), pale yellow hexagonal plates, m.p. 140-141° (decomp.) (Found: C, 59.1; H, 4.5; N, 8.7. \( \text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_8 \) requires C, 59.1; H, 4.5; N, 9.0%). \( \nu_{\max} \) 1720br, 1608w, 1558, 1547, 1504, 1434, 1413 cm\(^{-1} \). (CHCl\(_3\) soln.).

The pyrazoline (10 mg.) was heated to 150° in an oilbath for 5 min. The resulting melt was triturated with methanol and the methanol was evaporated, giving an oil which solidified on drying in vacuo, \( \nu_{\max} \) 1721, 1600w, 1560w, 1510, 1435 cm\(^{-1} \) (CHCl\(_3\) soln.), mass spectrum almost identical to that of the pyrazoline. T.l.c. showed the presence of several components, the slowest-moving having an \( R_f \) equal to that of the pyrazoline.

**Attempted Methylation of the Quinoline (97).**

The quinoline (97) (80 mg.) in dimethyl formamide (10 ml.) (dried over calcium hydride) was added to a stirred suspension of sodium hydride (50% dispersion in oil, 0.2g.) in dimethyl formamide (20 ml.). The mixture was then boiled under reflux, methyl iodide (1 ml., dried over calcium hydride) in dimethyl formamide (10 ml.) was added dropwise, and boiling was continued for \( \frac{1}{2} \) hr. with stirring. The mixture was cooled, methanol was added to destroy unreacted sodium hydride and the mixture was poured into water (200 ml.). The aqueous mixture was extracted with chloroform (4x100 ml.) and the combined
chloroform extracts were washed, dried and evaporated. The residue was dissolved in methanol and the solution on cooling gave impure starting material (50 mg.), m.p. 130-132°. 

Hydrogenation of the 2-Methylquinoline First Red Adduct.

(i) The red adduct (0.50g.) in glacial acetic acid (100 ml.) was shaken under hydrogen (5 atm.) with 5% palladium-on-charcoal (0.3g.) for 9 hr. The solution was filtered, the yellow filtrate was evaporated and residual acetic acid was removed by repeated addition and evaporation of methanol. The resulting yellow oil in methanol gave pale yellow crystals on cooling; these were collected and dissolved in methanol. This solution on cooling deposited straw-yellow crystals (40 mg.), which were collected and retained (A). The filtrate was concentrated, and on cooling gave the tetrahydro-derivative, hexamethyl 6,7,11,12,13,15,16,17-octahydro-9-azacyclopenta [a] phenanthrene-11,12,13,15,16,17-hexamethoxy (106) (40 mg.), colourless plates, m.p. 60-63° (Found: C, 58.7; H, 5.6; N, 2.3. C_{28}H_{31}NO_{12} requires C, 58.6; H, 5.5; N, 2.4%., ν_{max.} 1731 br, 1602 w, 1493 w, 1460 br, 1435 cm^{-1} (CHCl_{3} soln.). The crystals A on further recrystallisation from methanol gave a slightly impure sample of the tetrahydro-derivative (106) (20 mg.), m.p. 55°. 

(ii) The red adduct (0.50g.) in glacial acetic acid (100 ml.) was shaken under hydrogen (5 atm.) with Adams' catalyst (0.25g.) for 24 hr. The crude product, obtained
as above, was a white solid; this was triturated with methanol, giving crystalline material (150 mg.) which on further recrystallisation from methanol-acetone-tritile gave the hexahydro-derivative, hexamethyl 6,7,8,11,12,13,14,15,16,17-decahydro-9-azacyclopenta[a]phenanthrene-11,12,13,15,16,17-hexacarboxylate (104) (120 mg.), thick rods, m.p. 196-8° (lit. 195-197°) (Found: C, 58.6; H, 5.8; N, 2.5. Calc. for C_{28}H_{33}NO_{12}: C, 58.4; H, 5.8; N, 2.4%). v_{max}. 1730br, 1606, 1580, 1497, 1450br cm.^{-1}.

Attempted Reduction of the 2-Methylquinoline First Red Adduct with Sodium Amalgam.

A suspension of the red adduct (88a) (1.0g) in methanol (350 ml.) was boiled under reflux with vigorous stirring. Sodium amalgam (4%, 30g.) was added in portions and boiling was continued. After 40 min. all red adduct had dissolved; the solution was still red. A further quantity of sodium amalgam (30g.) was added and boiling was continued for 1 hr., during which time the solution turned yellow. The methanolic solution was decanted from the amalgam, diluted with water, adjusted to pH 3 with dilute sulphuric acid and extracted with chloroform (3x50 ml.); the residual aqueous layer was colourless. The combined chloroform extracts were washed, dried and evaporated and the tarry residue in chloroform was chromatographed on alumina (25 ml. in benzene). Three faint yellow-brown bands were eluted but yielded only
traces of tar. The column was run dry and extruded, and a tarry brown band was extracted with methanol; this yielded only tar.

**Attempted Oxidation of the 2-Methylquinoline First Red Adduct with Nitric Acid.**

The red adduct (88a) (1.0g.) suspended in 2N nitric acid (20 ml.) was heated under reflux at 100° for 1 hr. The red solution on cooling deposited a very small amount of red solid. This was collected and the filtrate extracted with chloroform (2x100 ml.). The combined chloroform extracts were washed, dried and evaporated, giving a small amount of dark oil which yielded no tractable solid. T.l.c. indicated the presence of at least two pale yellow-brown components; the material was not further examined.

**Reaction of 2,8-Dimethylquinoline with Dimethyl Acetylene-dicarboxylate in Acetonitrile.**

(i) 2,8-Dimethylquinoline (20g.) in acetonitrile (50 ml.) was added to the ester (46 ml.) in acetonitrile (150 ml.) and the mixture heated under reflux for 24 hr. The bulk of the acetonitrile was evaporated and the resulting oil was allowed to stand at room temperature for 3 months. The remaining acetonitrile was evaporated, the thin, tarry residue was dissolved in benzene and the solution was divided into two equal portions, each of which was chromatographed on alumina (750 ml.) (in benzene). The
first eluates from both columns yielded tar containing unreacted ester. Continued elution of a yellow band in both cases gave tetramethyl 4a,10-dimethyl-4aH-benzo-[c]quinolizine-1,2,3,4-tetracarboxylate (54) (combined yield 1.0g.), thin yellow rods (from methanol), m.p. 98-100° (Found: C, 62.2; H, 5.5; N, 3.1. C_{23}H_{23}NO_{8} requires C, 62.6; H, 5.3; N, 3.2%), ν_{max.} 1751, 1745, 1718, 1641, 1631, 1580, 1552, 1439 cm^{-1}.

Further elution of an orange band yielded tetramethyl 10,11-dihydro-1-methylazepino[1,2-a]quinoline-7,8,9,10-tetracarboxylate (60) (combined yield 0.61g.), yellow-orange rods (from methanol), m.p. 158-159.5° (Found: C, 63.0; H, 5.3; N, 3.2. C_{23}H_{23}NO_{8} requires C, 62.6; H, 5.3; N, 3.2%), ν_{max.} 1760, 1743, 1730, 1673, 1634, 1606w, 1567, 1440, 1430, 1419 cm^{-1}. The mother liquors later deposited mixed crystals of the quinolizine (54) and the azepine (60) (1.3g.), from which pure quinolizine (0.4g.) and azepine (0.6g.) were isolated by fractional crystallisation from methanol (the azepine being the less soluble component).

Further elution of a red band yielded a mixture of the first and second red adducts (89a,b) (combined yield 1.0g.); the n.m.r. spectrum indicated first:second ca. 3:1 (unchanged after repeated attempts at fractional crystallisation). The columns were then run dry, extruded and dark blue bands extracted with chloroform-acetone. The combined extracts yielded the 2,8-dimethylquinoline blue adduct (Part 2) (0.29g.), deep blue prisms (from
methanol), m.p.272-274° (turning green) (lit.\(^7\) 274-276°)
(Found: C, 59.2; H, 4.8; N, 2.1. Calc. for \(C_{34}H_{31}NO_{15}\):
C, 58.9; H, 4.5; N, 2.0; and for \(C_{35}H_{33}NO_{15}\): C, 59.7;
H, 4.7; N, 2.0%). \(\nu_{\text{max}}\) 1739br, 1617, 1580w, 1542, 1441,
1414 cm\(^{-1}\) (CHCl\(_3\) soln.).

(ii) On another occasion (using 2,8-dimethylquinoline
(8.0g.) and the ester (19 ml.)) the crude reaction tar
was chromatographed on alumina (400 ml. in petrol).
First eluates yielded 2-(2,3-dimethoxycarbonyl-1-
ethyl)-8-methylquinoline (119) (1.4g.), colourless needles
(from methanol), m.p.107-107.5° (Found: C, 67.8; H, 5.7.
\(C_{17}H_{17}NO_4\) requires C, 68.2; H, 5.7%). \(\nu_{\text{max}}\) 1735, 1700,
1643w, 1593w, 1493w cm\(^{-1}\). Further elution of a pale
yellow band yielded the quinolizine (54) (0.5g.).

Further elution yielded yellow, red and dark-coloured
fractions; these eluates were combined and evaporated
and the residue in benzene-chloroform was chromatographed
on alumina (70 ml. in benzene). Elution of a pale red
band gave a tar which on standing in methanol yielded
crystals of the yellow adduct (144) (possible structure,
p. 69 ) (120 mg.), prisms, m.p.186-189° (Found: C, 60.0;
H, 5.0; N, 2.5. \(C_{29}H_{29}NO_{12}\) requires C, 59.7; H, 5.0;
N, 2.4%). \(\nu_{\text{max}}\) 1741, 1614w, 1573w, 1565w, 1546w, 1450,
1440 cm\(^{-1}\) (CHCl\(_3\) soln.).

Further elution of a dark-coloured band gave a
thick tar which on standing in methanol gave the phenol
2-(4-hydroxy-2,3,6-trimethoxycarbonylphenyl)-8-methyl-
quinoline (135) (alternative structure (137), p. 67 ).
(0.15 g.), yellow needles, m.p. 173-175° (175-176.5°, below)
(Found: C, 64.3; H, 4.9; N, 3.6; OMe, 22.6. C_{22}H_{15}NO_7
requires C, 64.5; H, 4.7; N, 3.4; 30Me, 22.8%), ν_{max.}
1731, 1720, 1615w, 1597, 1590, 1554w, 1496w cm^{-1}.

Further elution gave only tar. On subsequent
occasions no trace of the yellow adducts (135) and (144)
could be found by column chromatography or t.l.c.

**Reaction of 2,8-Dimethylquinoline with Dimethyl Acetylene-
dicarboxylate in Tetrahydrofuran.**

2,8-Dimethylquinoline (8.0 g.) in tetrahydrofuran
(20 ml., dried with lithium aluminium hydride as described\textsuperscript{11})
was added to the ester (19 ml.) in tetrahydrofuran (150 ml.),
and the mixture was boiled under reflux for 6 days.
After a further 3 days at room temperature the solvent
was evaporated and the residue in chloroform was chromo-
atographed on alumina (400 ml. in petrol). Elution of a
yellow band gave a tar which was retained (A). Further
elution of a red band gave a solid which on washing with
methanol and recrystallisation from methanol-acetonitrile
gave the first red adduct (89a) (150 mg.), prisms, m.p.
237-238° (lit.\textsuperscript{7} 224°). Further elution of a darker band
yielded a solid which after washing with methanol was
orange-red. On fractional crystallisation from methanol
this gave the phenol (135) (190 mg.), m.p. 175-176.5°
(after 2 recrystallisations from methanol-acetonitrile)
and then the first red adduct (89a) (100 mg.), m.p. 232-
234°. Further elution gave tar.
The tar A in chloroform was re-chromatographed on activated alumina (250 ml. in petrol). Elution of a pale yellow band yielded the colourless 1:1 adduct (119) (0.4g.), m.p. 105-106°C. Further elution gave tar.

**Reaction of 2,8-Dimethylquinoline with Dimethyl Acetylene-carboxylate in Methanol.**

2,8-Dimethylquinoline (19.2g.) in dry methanol (50 ml.) was added to the ester (46 ml.) in methanol (200 ml.), and the mixture was boiled under reflux for 24 hr. After 14 weeks at room temperature the dark crystals which had formed were collected and washed with methanol, and the filtrate and washings were combined, evaporated and retained (A). The crystals were recrystallised from methanol-acetonitrile to give the first red adduct, hexamethyl 1-methyl-11,12,13,17-tetrahydro-9-azacyclo[7]phenanthrene-11,12,13,15,16,17-hexacarboxylate (89a) (5.5g.), prisms, m.p. 237-8°C (Found: C, 59.9; H, 5.1; Calc. for C₂₉H₂₉NO₁₂: C, 59.7; H, 5.0%), νmax > 1751, 1741, 1699, 1632, 1516 br, 1430 cm⁻¹.

A was shown by t.l.c. to contain both first and second red adducts and the blue adduct, but was not chromatographed as further samples of these adducts were not in the event required.

**Reaction of the 2,8-Dimethylquinoline First Red Adduct (89a) with Bromine in Acetic Acid.**

The procedure was as for the 2-methylquinoline first
red adduct (p. 94), using the red adduct (89a) (2.0g.) and bromine (0.8 ml.). The crude reaction product in benzene-chloroform was chromatographed on alumina (200 ml. in 1:1 petrol:benzene). Elution of a faint yellow band yielded only a trace of tar. Further elution of the main yellow band gave a tar which was dissolved in methanol. After several weeks at room temperature the solution deposited pale yellow, amorphous crystals (70 mg.) which were recrystallised from methanol-acetonitrile to give prisms (40 mg.), m.p.182-183°, λ max. (λ) (optical densities in parentheses) 251(1.5), 290inf1(0.58), 300inf1(0.50), 366(0.40); n.m.r.: ArH, 2.05broad, 2.5-2.9 m; one(?) proton, ca.5.0d; ester Me, 6.0-6.4 m; C2 and Ar-Me, 6.77s, 7.13s, 7.35-7.5 m (a mixture: see p. 47).

**Reaction of the 2,8-Dimethylquinoline First Red Adduct (89a) with Zinc in Acetic Acid.**

The procedure was as for the 2-methylquinoline first red adduct (p. 96), using the red adduct (89a) (2.0g.). The crude reaction product in benzene was chromatographed on alumina (110 ml. in benzene). Elution of a pale yellow band yielded only a trace of tar. Further elution of a second yellow band gave an oily solid, which after two recrystallisations from methanol yielded white crystals (60 mg.), m.p.227-260°. These were not further investigated.

**Hydrogenation of a Mixture of the 2,8-Dimethylquinoline Red Adducts.**

A mixture of the red adducts (89a,b) (0.5g.) suspended
in methanol (100 ml.) was shaken under hydrogen (4.6 atm.) with Adams' catalyst (0.3g.) for 43 hr., and the red solution was filtered and evaporated. The red solid was triturated with methanol and the mixture filtered; the filtrate slowly deposited impure crystals of Gagan's hexahydro-derivative, \( \text{hexamethyl} 6,7,8,11,12,13,14,15,16,17\)-decahydro-1-methyl-9-azacyclopenta[a]phenanthrene-11,12,13,15,16,17-hexacarboxylate (105) (60 mg.), m.p. 165-170° (lit. 190°), \( \nu_{\text{max}} \) 1750br, 1603w, 1491, 1448 cm.\(^{-1}\) (CHCl\(_3\) soln.).

Attempted Reduction of the 2,8-Dimethylquinoline First Adduct with Sodium Amalgam.

The procedure was as for the 2-methylquinoline adduct (p. 100), using the 2,8-dimethylquinoline first red adduct (89a) (1.0g.). The crude reaction product in benzene-chloroform was chromatographed on alumina (40 ml. in benzene). Three faint yellow bands were eluted, but these gave only traces of tar. The column was run dry and extruded, and a tarry brown band was extracted with acetone-chloroform-methanol; this yielded only tar, and dark, tarry material remained adsorbed on the alumina.

Reaction of 2,6,8-Trimethylquinoline with Dimethyl Acetylenedicarboxylate in Acetonitrile.

2,6,8-Trimethylquinoline (10g.) in acetonitrile (30 ml.) was added to the ester (22 ml.) in acetonitrile (120 ml.), and the mixture was boiled under reflux for 6 days.
After a further 7 weeks at room temperature the acetonitrile was evaporated and the tarry residue in benzene-chloroform was chromatographed on alumina (700 ml. in petrol). First eluates smelled of unreacted 2,6,8-trimethylquinoline. Elution of a very pale yellow band yielded 2-(2,3-dimethoxycarbonylprop-1-enyl)-6,8-dimethylquinoline (120) (0.96 g.), colourless plates (from methanol), m.p. 107-108° (Found: C, 69.0; H, 6.3. C₁₈H₁₉NO₄ requires C, 69.0; H, 6.1%), ν max. 1737, 1713 br, 1642 w, 1618 w, 1589 w, 1452, 1434 br cm⁻¹.

Further elution of a deep yellow band gave the yellow adduct (145) (possible structure, p. 67) (100 mg.), parallelepipeds (from methanol-acetonitrile), m.p. 193.5-201° (Found: C, 60.9; H, 5.4; N, 2.3. C₃₀H₃₁NO₁₂ requires C, 60.3; H, 5.2; N, 2.3%), ν max. 1736 br, 1713, 1634 w, 1600, 1567, 1559, 1437 cm⁻¹. Further elution of a red band gave the first red adduct, hexamethyl 1,3-dimethyl-11,12,13,17-tetrahydro-9-azacyclopenta[a]phenanthrene-11,12,13,15,16,17-hexacarboxylate (90a) (0.78 g.), deep crimson rods (from methanol-acetonitrile), m.p. 224° (Found: C, 60.1; H, 5.3; N, 2.5. C₃₀H₃₁NO₁₂ requires C, 60.3; H, 5.2; N, 2.3%), ν max. 1749, 1740, 1688, 1622, 1609, 1573 w, 1523, 1430 cm⁻¹. The mother liquors yielded a further crop of the yellow adduct (145) (0.16 g.).

Further elution of a thin, deep red band yielded the second red adduct (90b) (80 mg.), bright red needles (from methanol-acetonitrile), m.p. 252-252.5° (Found: C, 60.2; H, 5.2; N, 2.3. C₃₀H₃₁NO₁₂ requires C, 60.3;
H, 5.2; N, 2.3%), $\nu_{\text{max.}}$ 1743, 1739, 1692, 1630, 1521 cm$^{-1}$.

Further elution of a blue band yielded very dark crystals (30 mg.) which were washed with methanol; this product was the 2,6,8-tri-methylquinoline blue reduct (Part Two), tiny rods, m.p. 272-276° (Found: C, 59.7; H, 4.7; N, 2.1.

$\text{C}_{35}\text{H}_{33}\text{N}_{15}$ requires C, 59.4; H, 4.7; N, 2.0 and $\text{C}_{36}\text{H}_{33}\text{N}_{15}$, C, 59.9; H, 4.9; N, 1.9%), $\nu_{\text{max.}}$ 1737, 1728, 1603, 1535 br, 1432 cm$^{-1}$ (CHCl$_3$ soln.).

Reaction of 2,6,8-Trimethylquinoline with Dimethyl Acetylene-dicarboxylate in Tetrahydrofuran.

2,6,8-Trimethylquinoline (2.0 g.) in dry tetrahydrofuran (10 ml.) was added to the ester (4.3 ml.) in tetrahydrofuran (40 ml.), and the mixture was boiled under reflux for 6 days. After 9 weeks at room temperature the yellow-orange solution was evaporated and the residue in benzene was chromatographed on alumina (200 ml. in petrol). First eluates yielded unreacted 2,6,8-trimethylquinoline (ca. 1 g.). Two pale yellow bands were then eluted, but each yielded only a small amount of tar.

Reaction of 2,4-Dimethylquinoline with Dimethyl Acetylene-dicarboxylate in Methanol.

2,4-Dimethylquinoline (8.2 ml.) in dry methanol (20 ml.) was added slowly with swirling to the ester (19 ml.) in methanol (150 ml.), and the mixture was kept at 0° for 24 hr. After 3 months at room temperature, the supernatant was decanted from the tar which had formed, the tar was
washed with methanol and the combined washings and supernatant were evaporated and retained (A).

The tar (19g.) in benzene-chloroform was chromatographed on alumina (570 ml. in benzene). Elution of a pale yellow band yielded dimethyl fumarate (100 mg.). Further elution of a yellow band yielded only a trace of dark tar. Further elution of a deep red band gave a tar, from which was isolated by crystallisation from methanol the red adduct (110) (structure, p. 52) (90 mg.), deep red, matted rods, m.p.143-147° (Found: C, 58.1; H, 5.0; N, 2.0. C_{35}H_{35}NO_{16} requires C, 57.9; H, 4.9; N, 1.9%), v_max. 1729br, 1610br w, 1540, 1518, 1482, 1435, 1405w cm.^{-1}. Further elution gave intractable tar.

A in chloroform was chromatographed on alumina (450 ml. in benzene). The material was irreversibly adsorbed as a tarry brown band, and the column was discarded.
PART FOUR

Reaction of 2,4,6,8-Tetramethylquinoline with Dimethyl Acetylenedicarboxylate.

2,4,6,8-Tetramethylquinoline (71g.) in acetonitrile (100 ml.) was added to the ester (125 ml.) in acetonitrile (600 ml.) and the mixture was boiled under reflux for 1 week. After a further week at room temperature, the acetonitrile was evaporated and the tarry residue was allowed to stand at room temperature for 2 months, during which time a large amount of solid was formed. Methanol was added; the following day the solid was collected and washed with methanol, and the washings and filtrate were combined, evaporated and retained (A).

The solid was a mixture of thick, brown crystals and fine yellow ones; these were readily separated as the yellow but not the brown crystals adhered to the damp filter paper. The yellow crystals on recrystallisation from methanol-acetonitrile gave the yellow adduct (16) (possible structure, p. 69) (1.9g.), thick prisms, m.p.216-216.5° (Found: C, 61.3; H, 5.4; N, 2.3. C_{31}H_{33}NO_{12} requires C, 60.9; H, 5.4; N, 2.3%), \nu_{max.} 1744, 1731, 1713, 1603, 1568, 1430 cm^{-1}. The brown crystals on recrystallisation from acetonitrile gave 2-(2,3-dimethoxycarbonylprop-1-enyl)-4,6,8-trimethylquinoline (12) (13.3g.), pale brown needles, m.p.136.5-137.5° (Found: C, 69.8; H, 6.5; N, 4.3. C_{19}H_{21}NO_{4} requires C, 69.7; H, 6.5; N, 4.3%), \nu_{max.} 1740, 1712, 1640, 1620, 1597, 1493,
1450, 1439, 1408 cm$^{-1}$. The mother liquors from the brown crystals later deposited crops of the yellow adduct (146) (0.5g.) and then the pale brown adduct (121) (0.5g.).

A in benzene-chloroform was applied in equal portions to two alumina chromatography columns (each 1800 ml. in benzene); yellow and then deep orange bands were eluted from these columns. The combined eluates from the two yellow bands yielded 2-[4-(cis-1',2'-dimethoxycarbonyl-vinylxy)-2,3,6-trimethoxycarbonylphenyl]-4,6,8-trimethylquinoline (124) (alternative structure, p. 61) (2.7g.), flocculent, very fine white rods (from methanol-acetonitrile), m.p.194.5-196.5° (Found: C, 62.4; H, 5.2; N, 2.6 C$_{30}$H$_{29}$N$_{11}$O$_{11}$ requires C, 62.2; H, 5.0; N, 2.4%), v$_{max}$. 1741, 1722, 1645, 1597 w, 1410 w cm$^{-1}$. The combined eluates from the deep orange bands yielded mixed crystals which on fractional crystallisation from methanol-acetonitrile gave first the yellow adduct (146) (1.3g.) and then a further crop of the white adduct (124) (3.0g.).

The mother liquors from the crystallisations described in the preceding paragraph were combined and evaporated, and the resulting tar in benzene was applied in equal portions to two alumina chromatography columns (each 2 l. in 1:1 petrol (b.p.40-60°):benzene). First eluates from both columns yielded unreacted 2,4,6,8-tetramethylquinoline (combined weight 4.5g.), m.p.82-84° (lit.$^{14,5}$ 86°). Further elution of a pale yellow band yielded a white solid (total 1.6g.), which on recrystallisation from methanol gave the 1:1 adduct (121) (0.9g.) as off-white rods,
m.p. 136-137°. The mother liquor was evaporated and the residue after two recrystallisations from hexane gave the 1:1 adduct (122) (alternative structure, p. 59) (140 mg.), white needles, m.p. 100-101° (Found: C, 69.9; H, 6.2; N, 4.4. \( \text{C}_{19}\text{H}_{21}\text{NO}_{4} \) requires C, 69.7; H, 6.5; N, 4.3%), \( \nu_{\text{max.}} \) 1717, 1631w, 1619w, 1595w, 1567w, 1561w, 1435, 1412 cm.\(^{-1}\). Further elution of a slightly deeper yellow band yielded the adduct (121) (total 0.88 g.) as pale, straw-coloured rods, m.p. 135-137°. Further elution of a large, deep yellow band gave tetramethyl 4a,6,8,10-tetramethyl-4aH-benzo[c]quinolizine-1,2,3,4-tetracarboxylate (57) (17 g.), pale yellow prisms (from methanol), m.p. 151-153° (Found: C, 64.0; H, 5.6; N, 3.1. \( \text{C}_{25}\text{H}_{27}\text{NO}_{8} \) requires C, 64.0; H, 5.8; N, 3.0%), \( \nu_{\text{max.}} \) 1740, 1709, 1623, 1601w, 1539, 1456, 1433 cm.\(^{-1}\). Further elution of a deep red band gave brownish-yellow crystals; these gave the yellow adduct (146) (70 mg.) on recrystallisation from methanol-acetonitrile.

This reaction was first carried out on a much smaller scale (12 g. 2,4,6,8-tetramethylquinoline). The adduct (121) (2.3 g.) was isolated from the crude reaction mixture. Chromatography on alumina (700 ml. in benzene) then gave (in order of elution) the white adduct (124) (0.60 g.) and the yellow adduct (146) (0.53 g.). The adducts (57) and (122) were not isolated.

The adducts (121), (122) and (124) did not form methiodides on treatment with methyl iodide in boiling acetonitrile.
Hydrogenation of the Maleate Adduct (124).

(i) The adduct (124) (0.5g.) in glacial acetic acid (150 ml.) was shaken under hydrogen (5 atm.) with 10% palladium-on-charcoal (0.3g.) for 48 hr. The solution was filtered and evaporated, and residual acetic acid was removed by repeated addition and evaporation of methanol. The resulting pale yellow oil in methanol gave dirty white crystals, which on recrystallisation from methanol-acetonitrile (with decolourising charcoal) gave 2-[4-(1',2'-dimethoxycarbonyl)ethoxy]-2,3,6-trimethoxycarbonylphenyl]-4,6,8-trimethylquinoline (126) (alternative structure, p. L1) (0.34g.), brilliant white needles, m. p. 160-162° (Found: C, 61.8; H, 5.4; N, 2.4. \( \text{C}_{30}\text{H}_{31}\text{N}_2\text{O}_{12} \) requires C, 62.0; H, 5.4; N, 2.4%), \( \nu_{\text{max}} \) 1752, 1737, 1721, 1615w, 1590, 1574w, 1558w, 1440, 1414w cm\(^{-1}\).

(ii) The adduct (124) (0.3g.) in glacial acetic acid (100 ml.) was shaken under hydrogen (5 atm.) with Adams' catalyst (0.15g.) for 24 hr. The crude product, isolated as in (i), yielded the phenol 2-(4-hydroxy-2,3,6-trimethoxycarbonylphenyl)-4,6,8-trimethylquinoline (127) (alternative structure, p. L1) (50 mg.), pale yellow rods (from methanol), m. p. 152-156° (Found: C, 66.1; H, 5.3; N, 3.3. \( \text{C}_{24}\text{H}_{23}\text{NO}_7 \) requires C, 65.9; H, 5.3; N, 3.2%), \( \nu_{\text{max}} \) 1730, 1600w, 1583w, 1554w, 1540w, 1485w, 1437 cm\(^{-1}\) (CHCl\(_3\) soln.).
(iii) The procedure of (ii) was repeated, using the adduct (124) (0.5 g.) and a newly-opened batch of Adams' catalyst (0.25 g.). The product was the reduced phenol (128) (p. 123) (120 mg.), brown rods (from methanol), m.p. 156-160°, \( \nu_{\text{max.}} \) 1738, 1721, 1581 cm\(^{-1}\). T.l.c. showed the presence of impurities, but the material was not further purified.

**Methylation of the Reduced Phenol (128).**

The impure phenol (128) (100 mg.) in methanol (15 ml.) was treated with ethereal diazomethane (generated from N-methyl-N-nitrosourea\(^{112}\)) until a yellow colour persisted. After 2 hr. glacial acetic acid was added to decompose unreacted diazomethane, the almost colourless solution was evaporated, and residual acetic acid was removed by repeated addition and evaporation of methanol. The residue in methanol gave on cooling the methoxy-compound (129) (p. 123) (40 mg.), white prisms, m.p. 141-142°, \( \nu_{\text{max.}} \) 1736, 1728, 1590br, 1479w, 1460w, 1451w, 1436w, 1416br w(CHCl\(_3\) soln.). T.l.c. again showed the presence of impurities, which were still present after recrystallisation from methanol.

**Methylation of the Phenol (135) from 2,8-Dimethylquinoline.**

The phenol (135) (100 mg.) was methylated by the above procedure, giving 2-(4-methoxy-2,3,6-trimethoxy carbonyl phenyl)-8-methylquinoline (136) (alternative structure (138), p. 127) (70 mg.), white needles (from methanol), m.p. 168-171° (Found: C, 65.3; H, 5.1; N, 3.4. \( \text{C}_{23}\text{H}_{21}\text{NO}_7 \) requires C, 65.2; H, 5.0;
Reduction of the Maleate Adduct(124) with Zinc in Acetic Acid.

Zinc dust (2g.) was added in portions to a vigorously-stirred solution of the adduct (124) (1.0g.) in glacial acetic acid (50 ml.) and stirring was continued for 1 hr. The solution was filtered, the yellow filtrate was diluted with water (100 ml.) and extracted with chloroform (1x100 ml., 1x50 ml.), and the combined chloroform extracts were washed, dried and evaporated. Residual acetic acid was removed by repeated addition and evaporation of benzene, and the residue in benzene was chromatographed on alumina (100 ml. in benzene).

Elution of a pale yellow band yielded only tar. Further elution of the main yellow band yielded a yellow tar which deposited yellow crystals on trituration with methanol; these were collected and retained (A). The mother liquor on cooling deposited a further crop of yellow crystals (55 mg.), which after recrystallisation from methanol gave the reduction product(130) (possible structure, p. 64__) (40 mg.), thick, yellow rods, m.p. 224-227° (Found: C, 65.5; H, 6.1; N, 3.2. \( \text{C}_{24}\text{H}_{27}\text{NO}_{7} \) requires C, 65.3; H, 6.2; N, 3.2%), \( \nu_{\text{max.}} \) 1738, 1732, 1711, 1602, 1550br, 1540 cm. \(^{-1} \).

The crystals A (110 mg.) on recrystallisation from methanol-acetonitrile gave an impure sample of the reduction
product (130) (40 mg.), m.p. ca. 200°; t.l.c. showed
the presence of a second, faster-moving yellow component.

Bromination of the Maleate Adduct (124).

A stirred solution of the adduct (124) (1.0 g.) in
boiling glacial acetic acid (50 ml.) was treated dropwise
with bromine (0.4 ml.) in acetic acid (5 ml.), and boiling
was continued for 5 min. with stirring. The solution was
wine-red but turned yellow on standing. Accordingly it
was reheated and bromine (0.8 ml.) in acetic acid (7 ml.)
was added dropwise. After a further 5 minutes' boiling
and stirring, the solution was evaporated and residual acetic
acid was removed by repeated addition and evaporation of
benzene. The resulting yellow tar in benzene was chromato-
graphed on alumina (60 ml. in benzene). The first eluates
were colourless and gave a white solid (190 mg.) on evap-
oration. Several recrystallisations from methanol gave
white prisms (20 mg.), m.p. 147-151° (principal component
probably the dibromo-compound (131), p. 65°), \( \lambda_{\text{max}} \) (M)
(optical densities in parentheses) 269(0.68), 307(0.28);
(MA) 261(0.81), 331(0.23); n.m.r.: ArH, 2.15 s, 2.6-2.7 m;
-\( \text{CEBr.CHEBr} \), 3.32 s; ester Me, 6.13-6.35, 6.57-6.64 m; -\( \text{CH}_2\text{Br} \),
6.88 s; Ar-Me, 7.3-7.5 m (CDCl\textsubscript{3} soln.); m/e ca. 740 (faint \( \text{Br}^- \) -
triplet), 659(24%), 657(23), 644(30), 642(47), 628(22), 627(23),
626(23), 625(20), 600(60), 598(58), 564(43), 548(23), 520(100),
492(26), 341(32), 324(41), 310(28), 117(29), 96(88), 94(86),
91(83), 82(27), 80(26), 59(38) (others< 20%). T.l.c. showed
the presence of several components. The mother liquors gave
Further crops of white prisms (100 mg.) whose n.m.r. spectra were very similar to the above spectrum.

Further elution of a thin, yellow band gave a yellow, crystalline mixture of brominated phenols (p. 258) (10 mg.), m.p. 207-211° (from methanol-acetonitrile), \( \lambda_{max} \) (M) (optical densities in parentheses) 255(0.85), 310(0.37), 340 inf. (0.24); (MA) 253(1.07), 329(0.26); (S) 254 br(0.38), 311 br(0.43), 350 inf. (0.24) (colourless); n.m.r.: ArH(3), 2.40 s, 2.53 s (broad); ester CH\(_3\), 6.08, 6.20 (6); CH\(_2\)?, 6.88; Ar-Me, 7.24-7.50 m (CHCl\(_3\) soln., approximate integration); m/e 597 (27%), 595 (46), 593 (30), 565 (20), 563 (40), 561 (14), 517 (91), 515 (100), 500 (19), 486 (33), 485 (60), 484 (48), 483 (50), 482 (20), continuous series of peaks below 460 (sample decomposed).

Photochemical Isomerisation of the Yellow Adduct (146).

The adduct (146) (0.50 g.) in methanol (700 ml.) was irradiated for 1 hr. The methanol was evaporated (using a water-bath of temperature ca. 35°) and the residue in benzene-chloroform was chromatographed on alumina (20 ml.). Elution of a yellow-band gave an oil, which on trituration with methanol gave the photo-isomer (structure, p. 72) (50 mg.), rods, m.p. 260-262° (Found: C, 60.6; H, 5.5; N, 2.3. C\(_{31}\)H\(_{33}\)NO\(_{12}\) requires C, 60.9; H, 5.4; N, 2.3%), \( \nu_{max} \) 1740 br, 1641 w, 1617, 1458 w, 1449, 1432 cm\(^{-1}\) (CHCl\(_3\) soln.).
Attempted Reduction of the Yellow Adduct (146) with Zinc in Acetic Acid.

Zinc dust (2g.) was added in portions to a vigorously-stirred solution of the adduct (146) (1.0g.) in warm glacial acetic acid (50 ml.), and stirring was continued for 1½ hr. The work-up procedure of p. 26 gave unreacted starting material (0.74g.).

Attempted Hydrogenation of the Yellow Adduct (146).

(i) The adduct (146) (0.40g.) in glacial acetic acid (100 ml.) was shaken under hydrogen (5 atm.) with 10% palladium-on-charcoal (0.25g.) for 24 hr. The solution was filtered and evaporated, and residual acetic acid was removed by repeated addition and evaporation of methanol. The resulting yellow-brown solid (0.4g.) was triturated with methanol, giving crystals of unreacted starting material (0.11g.).

(ii) The adduct (146) (0.50g.) in glacial acetic acid (150 ml.) was shaken under hydrogen (5 atm.) with Adams' catalyst (0.25g.) for 24 hr. The crude yellow solid (0.5g.) obtained as above but without further purification with methanol, showed only one spot on t.l.c. (Rf = that of starting material) and had an i.r. spectrum identical to that of the starting material.
PART FIVE

Although the blue adducts are discussed in Part Two, two experiments with the 2-methylquinoline blue adduct are conveniently described here.

Reduction of the 2-Methylquinoline Blue Adduct with Bromine in Acetic Acid.

The blue adduct (2.0 g., prepared by D.R. Harrison) in boiling glacial acetic acid was treated dropwise with bromine (0.8 ml.) in acetic acid (8 ml.), and boiling was continued for 3 min. The solution was evaporated, residual acetic acid was removed by repeated addition and evaporation of chloroform, and the resulting deep green tar in benzene-chloroform was chromatographed on alumina (200 ml. in benzene). Elution of two brown bands gave tars. Further elution of a blue band gave a solid which on recrystallisation from methanol-acetonitrile gave an isomer of the blue adduct (120 mg.), dark green rods, m.p. 218.5-219° (Found: C, 58.6; H, 4.4; N, 2.0.

\( \text{C}_{33}\text{H}_{29}\text{NO}_{15} \) requires C, 58.3; H, 4.3; N, 2.1 and \( \text{C}_{34}\text{H}_{31}\text{NO}_{15} \) C, 58.9; H, 4.5; N, 2.0%), \( \nu_{\text{max}} \) 1740, 1715, 1632, 1609, 1561, 1548, 1525, 1433, 1421 cm\(^{-1}\).

Further elution of a second blue band gave a dark solid, which on recrystallisation from methanol-acetonitrile gave starting-material (80 mg.), m.p. 252-254°. Further elution gave dark tar.
Attempted Reduction of the 2-Methylquinoline Blue Adduct
with Zinc in Acetic Acid.

Zinc dust (2g.) was added in portions to a vigorously-
stirred solution of the blue adduct (2.0g.) in boiling
glacial acetic acid (100 ml.), and stirring was continued
for ½ hr. with gentle heating. The solution was filtered,
the yellow filtrate was diluted with water (100 ml.) and
extracted with chloroform (2x100 ml.), and the combined
chloroform extracts were washed, dried and evaporated.
Residual acetic acid was removed by repeated addition
and evaporation of methanol, and the residue in methanol
gave yellow crystals (0.42g.) on cooling. Recrystallisation
from methanol gave yellow-green prisms (0.30g.), m.p. ca.
210°. The n.m.r. spectrum of this product showed aromatic
proton resonances (1.75-1.9m, 2.1-2.75m) and ester-methyl
resonances (5.8-6.5 m) (CDCl₃ soln.), but a mass spectrum
was identical to that of dimethyl fumarate. A repeat mass
spectrum however showed a continuous series of peaks at
all mass numbers from ca. 590 downwards, and thus the
material appears to have been polymeric ester. The crystals
darkened on standing, and in solution rapidly gave tarry
brown colours.
TABLES 9 - 11

u.v., n.m.r. and mass spectra

(The spectral data for a few compounds and mixtures of uncertain constitution are included at the appropriate points in the Experimental Section.)
**TABLE 9**

Ultra Violet Absorption Spectra

M = methanol; MA = methanol acidified with 3 drops of 72% perchloric acid; P = MeOH-72% perchloric acid (2:1 v/v); Q = MeOH-72% perchloric acid (1:1 v/v); B = MeOH-0.2N NaOH soln. (1:1 v/v).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent</th>
<th>$\lambda_{\text{max.}}$ (nm) ($10^{-4} \epsilon$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(28) ^45</td>
<td>M</td>
<td>265 (1.59), 276 (1.85), 296 (2.21), 307 (2.25), 320 (1.60), 400infl. (0.80), 424 (1.22), 448 (1.19), 480infl. (0.57)</td>
</tr>
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<td>P</td>
<td>228 (6.07), 242 (4.25), 322 (1.36)</td>
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<td>M</td>
<td>223 (2.24), 274 (1.62), 283 (1.60), 307infl. (1.81), 317 (1.94), 331 (1.55), 420infl. (0.76), 440 (0.99), 464 (0.98), 498infl. (0.51)</td>
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<td>M=</td>
<td>212 (2.74), 265infl. (4.23), 271 (4.55), 330 (1.44)</td>
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<td>M</td>
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<td>M*</td>
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<tr>
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<td>M*</td>
<td>250 (1.96), 299infl. (0.63), 398 (0.62)</td>
</tr>
<tr>
<td>(54)</td>
<td>M*</td>
<td>261 (1.88), 381 (0.53)</td>
</tr>
<tr>
<td>(55)</td>
<td>M*</td>
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<td>M*</td>
<td>262br (2.44), 307infl. (0.95), 395 (0.46)</td>
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<td>(57)</td>
<td>M</td>
<td>265 (1.90), 306infl. (0.37), 385 (0.58)</td>
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<tr>
<td>(58)</td>
<td>M</td>
<td>224 (2.12), 261infl. (0.73), 270 (0.87), 281 (1.02), 300 (1.07), 311 (1.16), 324 (0.83), 405infl. (0.67), 426 (0.90), 447 (0.85), 475infl. (0.47)</td>
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<td>P</td>
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<td>(59)</td>
<td>222 (2.80), 275 (1.50), 296 (1.94), 305 (1.92), 321 (1.52), 422 (1.00), 444 (1.00)</td>
<td>243 (3.19), 321 (1.26)</td>
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<td>(60)</td>
<td>226 (2.30), 264inf. (0.97), 272inf. (1.17), 281 (1.55), 304 (2.26), 314inf. (1.18), 326 (0.84), 398inf. (0.75), 418 (1.03), 440 (1.01), 466 (0.55)</td>
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<td>(61)</td>
<td>223 (2.96), 271inf. (1.45), 278 (1.65), 299 (2.37), 311 (2.18), 323 (1.61), 418inf. (0.68), 438 (0.89), 462 (0.86), 493inf. (0.45)</td>
<td>247 (4.28), 325 (1.21)</td>
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<td>(62)</td>
<td>240 (3.00), 254inf. (2.54), 322 (1.23), 334inf. (1.09), 446br (0.90), 468inf. (0.86)</td>
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<tr>
<td>(63)</td>
<td>262inf. (1.02), 272 (1.39), 292inf. (1.89), 300 (1.97), 320 (1.83), 406br (1.08), 424 (1.08), 449inf. (0.60)</td>
<td>253 (4.12), 337 (0.70)</td>
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<td>(64)</td>
<td>223 (2.78), 271 (1.27), 282 (1.41), 299 (1.31), 312 (1.43), 325 (1.10), 410inf. (0.90), 429 (1.13), 450 (1.08), 480inf. (0.57)</td>
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<tr>
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<td>227 (0.92), 277 (0.98), 379 (0.44)</td>
<td>223br (0.9), 275inf. (0.5), 390 (0.3)</td>
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<td>(66)</td>
<td>257 (0.93), 266 (1.30), 280 (1.65), 293inf. (1.59), 299 (1.80), 310 (1.93), 321 (1.37), 426 (1.04), 447 (1.03), 476inf. (0.58)</td>
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<td>(67)</td>
<td>245 (2.98), 304 (0.69), 316inf. (1.02), 323 (1.15), 326 (1.12)</td>
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<td>(68)</td>
<td>221 (2.52), 270inf. (1.33), 280 (1.55), 300inf. (1.70), 310 (1.83), 322 (1.35), 426 (1.06), 448 (1.05), 475inf. (0.50)</td>
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<td>(69)</td>
<td>244 (2.94), 316inf. (1.01), 323 (1.14)</td>
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<td>M</td>
<td>219 (2.4), 270infl. (1.5), 277 (1.6), 296 (1.4), 309 (1.5), 322 (1.1), 420 (0.8), 451 (0.8), 480infl. (0.4)</td>
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<td>M</td>
<td>220 (2.32), 260infl. (1.11), 27infl. (1.56), 278 (1.73), 299 (1.68), 311 (1.80), 325 (1.41), 412infl. (0.78), 431 (1.00), 455 (0.95), 482 (0.49)</td>
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<td>M</td>
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<td>242 (3.93), 322 (0.90)</td>
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<td>M</td>
<td>239 (2.65), 298br (1.27), 428br (0.52)</td>
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<td>P</td>
<td>24infl. (3.40), 301br (1.16), 437br (0.49)</td>
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<td>231 (0.88), 284 (0.42), 306infl. (0.32), 323 (0.25), 349infl. (0.42), 366 (0.92), 382 (1.26), 426infl. (0.42), 456infl. (0.77), 480 (0.99), 511 (0.87), 546infl. (0.40)</td>
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<td>266 (0.94), 327infl. (0.24), 366 (0.42), 383 (0.65), 448infl. (0.58), 472 (0.75), 501 (0.69), 534 (0.35)</td>
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<td>M</td>
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MA 260 (1.49), 286 infl. (1.97), 292 (2.13), 339 infl. (0.71), 372 (1.44)

(90b) M 240 (1.55), 285 (0.67), 318 (0.53), 332 (0.61), 368 (1.34), 384 (2.12), 453 infl. (1.29), 479 (2.02), 509 (2.14), 545 (1.11)

MA 296 (2.49), 369 infl. (1.74), 375 (1.91)

(96) M* 247 (3.42), 278 infl. (1.53), 285 infl. (1.31), 356 (0.96), 382 (0.54)

(97) M* 245 (3.48), 343 (0.92)

(100) M* 228 (2.62), 247 (3.48), 337 (0.98), 352 infl. (0.75)

(104) M 259 (0.89), 299 (0.18)

(105) M*, P 219 (1.25), 264 (0.50), 297 infl. (0.12)

(106) M 271 (1.47), 282 (1.57)

P 240 infl. (0.62), 271 (0.74), 288 (0.92)

(110) M 234 (2.24), 323 (1.00), 368 (2.30), 384 (3.09), 502 br (1.57)

MA 280 (2.40), 367 (2.10)

(119) MA 263 infl. (3.78), 270 (4.09), 326 (1.22)

2,8-Me₂-quinoline M 235 (4.08), 284 (0.40), 294 (0.39), 297 infl. (0.36), 306 (0.33), 311 (0.25), 314 infl. (0.21), 319 (0.30)

MA 246 (4.43), 300 infl. (0.34), 319 (0.60)

(120) M* 269 infl. (4.34), 275 (4.76), 338 (1.44)

2,6,8-Me₃-quinolinel M 236 infl. (4.19), 239 (4.29), 283 (0.35), 291 (0.34), 301 (0.29), 311 (0.28), 317 (0.23), 325 (0.27)

MA 248 (4.65), 309 infl. (0.59), 323 (0.73)

(121) M* 268 infl. (4.22), 275 (4.74), 334 (1.58)

2,4,6,8-Me₄-quinoline M 238 (5.43), 287 (0.49), 312 (0.32), 326 (0.32)

MA 248 (5.30), 322 (0.80)

(122) M 240 (2.77), 310 infl. (0.51), 317 (0.52), 331 (0.51)

MA 253 (3.46), 329 (0.86)
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<td>228infl. (2.02), 254 (1.61), 358 (0.88), 374 (0.13), 413 (0.70)</td>
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(146) M 236 (1.77), 256inf1.(1.33), 265inf1.
(0.77), 350 (0.73), 409 (0.66)
P 236 (1.73), 255 (1.48), 359 (0.62),
416 (0.77)

photo-
M 253inf1.(2.13), 260 (2.31), 277 (2.30),

isomer of
P 243 (1.17), 289 (2.08), 346inf1.(1.30),

(146) 287 (2.42), 334 (1.69)

359 (1.79)

br = broad, infl. = point of inflexion. * no change in P.
\( ^a \) No change in MA. \( ^b \) Measured by J.K.Stubbs. \( ^c \) Optical densities in parentheses.
TABLE 10
Nuclear Magnetic Resonance Spectra

\( \tau \)-values, \( J \) in Hz, for solutions in deuteriochloroform, with tetramethysilsilane as internal reference. An asterisk* indicates that the data were obtained in trifluoroacetic acid solution.

<table>
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<tr>
<th>Compound</th>
<th>Frequency (MHz)</th>
<th>Proton Assignments</th>
<th>Ester methyls</th>
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</thead>
<tbody>
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<td>(28)(^4,5)</td>
<td>60</td>
<td>( \text{ArH}(4), 2.5-2.7 \text{m}; \text{5-H}, 2.74 \text{d}; )</td>
<td>6.18, 6.29, 6.30, 6.30</td>
</tr>
<tr>
<td></td>
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<td>6-H, 2.32 \text{d}; ( J_5,6 = 9.5; \text{10-H} ), 6-H, 2.32 \text{d}; ( J_5,6 = 9.5; \text{11-H}_A ), ca. 6.4 \text{a}; 11-H(_C), 7.37m</td>
<td></td>
</tr>
<tr>
<td>(28)*(^4,5)</td>
<td>60</td>
<td>( \text{ArH}(4), 1.3-1.9 \text{m}; \text{5-H}, 0.60 \text{d}; )</td>
<td>5.81, 5.88, 5.88, 5.88</td>
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<td>6-H, 1.3-1.9m; ( J_5,6 = 8.5; \text{7-H} ), 5.88, 6.12</td>
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<td>4.12; 10-H, 11-H(_A), 6.0-6.5m; ( J_5,6 = 8.5; \text{11-H}_C), 7.2 \text{m}</td>
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<td>(29)(^4,5)</td>
<td>60</td>
<td>( 1-\text{H}, 3.68 \text{d}; )</td>
<td>6.22, 6.22, 6.22, 6.22</td>
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<td>2-\text{H}, \text{ca. 2.6m}; ( J_1,2 = 8.5; J_1,3 = 2 );</td>
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<td>2-H, \text{ca. 2.6m}; ( J_1,2 = 8.5; J_1,3 = 2 ); 2.49 \text{d};</td>
<td>6.28, 6.68</td>
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<td>5-H, 2.80 \text{d}; 6-H, 2.30 \text{d}; ( J_5,6 = 10 );</td>
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<td>10-H(_A), 7.2q; 10-H(_C), 6.7 \text{m}; ( J_5,6 = 10 );</td>
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<td>11-H(<em>B), 5.5q; ( J</em>{AB} = 8.4; J_{AC} = 13.5; )</td>
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<td>( J_{BC} = 11.5 )</td>
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<td>(39)(^4,5)</td>
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<td>( \text{ArH}(5) ) and vinyl-H, 1.7-2.1m;</td>
<td>6.11, 6.28</td>
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<td>side-chain CH(_2), 5.30</td>
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<tr>
<td>(51)(^4,5)</td>
<td>60</td>
<td>( \text{ArH}(4), 2.78; )</td>
<td>6.12, 6.19, 6.19</td>
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<td>( 4\text{-a-Me}, 8.51; )</td>
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<td>5-H, 6-H, 3.47</td>
<td>6.26, 6.31</td>
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<td>(52)</td>
<td>100</td>
<td>( \text{ArH}(4), 2.67-3.05 \text{m}; 4\text{-a-Me}, 8.56; 8.56; 6.18, 6.24, 6.24</td>
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<td>5-Me, 7.88; 6-H, 3.67 \text{d}</td>
<td>6.33, 6.51</td>
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<td>(53)</td>
<td>100</td>
<td>( \text{ArH}(4), 2.7-2.85 \text{m}; 4\text{-a-Me}, 8.56; 5-H, 3.74; 6-Me, 7.89</td>
<td>6.17, 6.23, 6.23</td>
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<td>8.56; 5-H, 3.74; 6-Me, 7.89</td>
<td>6.32, 6.39</td>
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<td>(54)</td>
<td>100</td>
<td>( \text{ArH}(3), 2.78-3.06 \text{m}; 4\text{-a-Me}, 8.60; 5-H, 6-H, 3.46; )</td>
<td>6.13, 6.18, 6.34, 6.62</td>
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<td>10-Me, 6.34, 6.62</td>
<td>7.63</td>
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(55) 100  
ArH(4), 2.33-2.43m, 2.65-6.15, 6.22, 2.93m; 4a-Me, 8.49; 5-H, 3.37 6.31, 6.39

(56) 60  
ArH(4) and 5-Ph, 2.7-2.9m; 4a-Me, 8.41; 6-H, 3.62 6.57, 6.77

(57) 60  
4a-Me, 8.68; 5-H, 3.77; 7,9-H, 3.11; Ar-CH₃, 6.25, 6.30, 6.45, 6.68

(58) 100  
ArH(4) and 5-H, 2.6-3.1m; 6-Me, 7.50; 10-H, 6.18, 6.29, 6.37

(59) 60  
60  ArH(4), 2.45-3.0m; 5-Me, 7.60; 6-H, 2.43; 10-H, 6.09-6.47m; 6.4m; 11-Hc, 7.44m

(60) 100  
1-Me, 7.65; ArH(3), 5-H, 2.7-6.23, 6.32

(61) 100  
ArH(4) and 6-H, 2.15-2.95m; 10-H, 6.2-6.57m; 6.34(9)

(62) 60  
ArH(4), 5-H and 6-Ph, 2.55-3.0m; 10-H, 6.18m; 11-Hc, 7.49m

(63) 100  
ArH(4) and 6-H, 2.4-2.95m; 4-H, 2.10d; 5-OMe, 5.93; 10-H, 6.2-6.57m; 6.34(9)

(64) 100  
1-H, 3.62d; J₁₂, 8.0; ArH(3) and 5-H, 2.75-3.14m; 6-Me, 7.47; 10-H, 7.24q; 11-Hc, 5.45g; 10-H, 6.61-6.84m; J₂₃AB, 8.3; J₁₂₃, 12.6; J₃₄BC, 10.3

(67) 60  
ArH(4) and Ph, 2.7-2.82m; 4a-PhCH₂, 6.75d; 7.15d, 6.34, 6.34
(68) 60 ArH(4) and 5-H, 2.6-3.0m; 6.23, 6.22, 6-H, 2.33d; J_{65} 9.5; 10,11-H, 6.30, 6.37 6.0-ca. 6.4m; d 11-Me, 8.38d; J_{11-H,11-Me} 7.6

(69) 100 ArH(4) and 5-H, 2.5-3.05m; CH_{2-H}(3), 5.5-6.0m; 6-H, 2.33d; J_{65} 9.5; 10-H, CH_{3-H}(12), 8.6-8.9m 6.14d; 11-H, 6.66m; J 11-Me, 8.35d; J_{10-H,11-H} 10.9; J_{11-H,11-Me} 7.7

(70) 60 ArH(9), 2.5-3.1m; 5-H, 6.20, 6.31, 3.37d; 6-H, 2.33d; J_{5,69} 6.59, 6.65 10-H, 4.87d; 11-H, 5.39d; J_{10,11} 10

(71) 60 1-H, 3.52d; J_{1,2} 8.5; ArH(3), 6.33, 6.33, 5-H, 2.62-3.25m; 6-H, 6.33, 6.73 2.45d; J_{65} 6.8; 10-H, 6.45- 6.96m; J 10-Me, 8.63d; J 7.3; 11-H, 5.78d; J_{10-H,11-H} 9.5

(85) 60 ArH(4), 2.85-3.23m; 6.19, 6.19, 4a-CHMe_{2}, 7.63; J_{4a-CH(4)} 2, 6.22, 6.31 9.03d, 9.07d; J 2.6; 5-H, 3.92d; J 6-H, 3.36d; J_{5,6} 10.3

(86) 60 1-CHMe_{2}, 7.93; J_{1-CH(4)} 2, 6.31, 6.31, 8.93d, 8.96d, J 6.7; 6.35, 6.42 ArH(4), 6-H, 2.52-3.15m; 5-H, 2.09d; J_{5,6} 10.7

(88a) 60 ArH(4), 2.7-3.1m; 6-H, 6.08, 6.23, 6.35 3.45d; 7-H, 2.99d; J_{7,6} 7 10.4; 11-H, 5.02d; 12-H, 6.10d; J_{11,12} 9.3; 17-H, 4.41

(88a)* 60 ArH(3), and 7-H, 1.48-2.0m; 1-H, 5.83, 6.02, 6.10, 2.19d; J_{1,2} 8.7; 6-H, 6.10, 6.19, 6.63 0.80d; J_{6,7} 9.6; 11-H, 4.54d; J_{11,12} 8.8; 12-H 5.7-6.2; J 16,17-H, 5.7-6.2K
(88b) 60  
ArH(4), 2.6-3.1m; 6-H, 6.12, 6.24, 6.31, 3.46d; 7-H, 2.89d; \( J_{6,7} ^{10,4} \); 6.33, 6.38, 6.40  
11-H, 5.32d; 12-H, 5.89d;  
\( J_{11,12} ^{8,7} \); 17-H, 4.81

(88b)* 60  
ArH(4) and 7-H, 1.2-2.0m; 6-H, 5.86, 5.92, 0.81d; \( J_{6,7} ^{8,8} \); 11-H, 4.74d; 6.01-6.26(12)  
12-H, 5.59d; \( J_{11,12} ^{7,7} \); 16,17-H, 5.8-6.3

(89a) 60  
ArH(3), 2.7-3.2m; 6-H, 6.11, 6.19, 6.31, 3.46d; 7-H, 2.99d; \( J_{6,7} ^{10,0} \); 6.40, 6.40, 6.68  
11-H, 5.12d; 12-H, 6.20d;  
\( J_{11,12} ^{8,4} \); 17-H, 4.51; 1-Me, 7.88

(89a)* 60  
ArH(3), 7-H, 1.6-2.1m; 5.9-6.3(15), 6-H, 0.89d; \( J_{6,7} ^{8,4} \); 11-H, 6.43  
4.56d; \( J_{11,12} ^{8,0} \); 12-H, 5.8-6.5; \( J_{16,17} ^{8,0} \); 5.8-6.5; \( J_{11,12} ^{10} \);  
1-Me, 7.31

(89b) 60  
ArH(3), 7-H, 2.7-3.2m; 6.1-6.5(18)  
6-H, 3.41d; \( J_{6,7} ^{10,5} \); 11-H, 5.47d; \( J_{12} ^{8,0} \); 12-H, 5.84d; \( J_{11,12} ^{10} \); 17-H, 4.95; 1-Me, 7.88

(89b)* 60  
ArH(3), 7-H, 4.98C; m

(90a) 60  
ArH(2), 3.10, 3.13; 6-H, 3.46d; 6.10, 6.18, 6.31, 7-H, 3.03d; \( J_{6,7} ^{10,0} \); 11-H, 6.39, 6.43, 6.67  
5.13d; 12-H, 6.20d; \( J_{11,12} ^{8,5} \); 17-H, 4.55; Ar-Me, 7.81, 7.91

(90a)* 60  
ArH(2), 7-H, 1.5-2.1m; 5.9-6.3(15), 6-H, 0.98d; \( J_{6,7} ^{8,7} \); 11-H, 6.47  
4.58d; \( J_{11,12} ^{8,7} \); 12-H, 5.8-6.5; \( J_{16,17} ^{8,0} \); 12-H, 5.61d; \( J_{11,12} ^{10} \);  
Ar-Me, 7.37(6)

(90b) 100  
ArH(2), 3.08; 6-H, 3.36d; 6.10, 6.30, 6.50, 7-H, 2.95d; \( J_{6,7} ^{10,0} \); 11-H, 6.39, 6.39, 6.52  
5.26d; \( J_{12} ^{8,0} \); 12-H, 5.61d; \( J_{11,12} ^{10} \); 17-H, 4.95; Ar-Me, 7.78, 8.03
(90b) * 60  
ArH(2), 1.98-2.15; 6-H, 5.89, 6.13, 6.13, 1.01d; 7-H, 1.86d; 6' 9.3; 11-H, 12-H, 4.98; 16,17-H, 5.9-6.5; Ar-Me, 7.36, 7.41
(96) 60  
ArH(4) and 5'-H, 2.15-2.9m; 5-H, 1.92m 6.27, 6.43
(96) * 60  
5'-H, 2.43; 6,7-H, 1.72br; 5.98, 5.98, 5-H, 1.1-1.5br m; 8-H, 2.98br 5.98, 6.19
(97) 60  
ArH(6) and 5'-H, 5.96, 6.25, 2.15-3.1m 6.31, 6.49
(97) * 60  
5'-H, 2.43; 3-H, 6.00, 6.00, 2.04d; 4-H, 0.86d; 8.9; 5,6,7-H, 1.53-1.9m; 8-H, 2.91br
(100) 60  
ArH(6) and >CHE, 2.2- 3.05m; -N-N-CH_2-, 4.45d, 4.74d, J ca. 2.7 and 5.02d, 5.32d; 8.0(integrates to 2 protons)
(104) 60  
1-H, 3.81d; J_{1,2} 7.6; 6.32-6.40(15), 2,3,4-H, 3.0-3.6m; 6.92
aliphatic H(11), 5.7-7.95m^a
(105) 60  
1-Me, 7.90; 2,3,4-H, 3.1-3.4m; 6.33-6.40(15), aliphatic H(11), 5.6-8.1m^a 7.03
(106) 60  
1-H, 3.76d; J_{1,2} 8.0; 6.30-6.38(15), 2,3,4-H, 2.9-3.55m; 6.73
aliphatic H, 5.9-7.14m(4)^a and 7.31br(4)
(110) 60  
ArH, 2.41(1) and 2.6-3.3(4); 6.18-6.42(24) 6-maleate H, 3.63; 6-CH_2, 6.1-6.4; 11-H, 5.32d; 12-H, 5.90d; J_{11,12} 9.0; 17-H, 4.78
(110) * 60  
ArH(5), 1.1-2.0m; 6-maleate 5.9-6.35(24) H, 2.78; 6-CH_2, 5.8-6.35; 11-H, 4.74d; 12-H, 5.58d; J_{11,12} ca. 8; 16,17-H, 5.8-6.35^k
(119)  100  ArH(5) and vinyl-H, 1.8-2.7m;  6.12, 6.30  
side-chain CH₂, 5.50;  8-Me, 7.25
(119)*  60  ArH(4) and vinyl-H, 1.7-2.22m;  5.96, 6.06  
4-H, 0.86d;  4, 8.5; side-chain  
CH₂, 6.21;  8-Me, 7.07
(120)  100  vinyl-H, 2.14; side-chain CH₂, 6.14, 6.33  
5.53;  3-H, 2.63d;  4-H, 2.03d;  
J 3, 8.4;  5, 7-H, 2.65br  
Ar-Me, 7.32, 7.55
(120)*  60  ArH(3) and vinyl-H, 5.93, 6.03  
1.7-2.1m;  4-H, 0.97d;  
J 3, 8.7; side-chain CH₂,  
5.20;  6-Me, 7.32;  8-Me, 7.10
(121)  100  vinyl-H, 2.12; side-chain CH₂, 6.13, 6.31  
5.50;  3-H, 3.71;  5, 7-H, 
2.43br,  2.59br; Ar-Me,  
7.30, 7.38, 7.50
(121)*  60  vinyl-H, 1.76; side-chain CH₂, 5.94, 6.04  
6.21; ArH(3), 1.85-2.16m;  
4-Me, 6.93;  6-Me, 7.31;  8-Me, 7.16
(122)  60  ArH, 1.84br(1), 2.64br(2);  6.16, 6.37  
fumarate-H, 2.95; side-chain  
CH₂, 6.71; Ar-Me, 7.29,  
7.34, 7.58
(122)*  60  ArH(3) and fumarate-H, 1.60(1), 5.93, 6.19  
2.1-2.3m; side-chain CH₂,  
6.46;  2(?)-Me, 6.92;  6-Me, 7.38;  
8-Me, 7.16
(124)  60  ArH(3), 2.41, 2.47, 2.62br;  6.07, 6.07, 6.20,  
Ar-Me, 7.30, 7.34, 7.50;  
5'-H, 2.16; maleate-H, 4.74
(124)*  60  ArH(3), 5'-H, 1.8-2.2m;  5.91, 5.91, 6.10  
4-Me, 6.91;  6-Me, 7.29;  
8-Me, 7.16; maleate-H, 3.67
(126)  60  ArH(3), 5'-H, 2.42-2.7m;  6.15, 6.17, 6.33,  
Ar-Me, 7.36, 7.36, 7.52;  
CHE.CH₂E, 4.81t; CHE.CH₂E, 
7.18d;  J 6.0
(127) 60  
\[ \text{ArH}(3), 5'-\text{H}, 2.4-2.72 \text{m}; \] 
\[ \text{Ar-Me}, 7.28, 7.34, 7.50 \alpha \] 
6.13, 6.15, 6.25

(128) 60  
\[ 3-\text{H}, 2.92; 5'-\text{H}, 2.56; \] 
\[ 4-\text{Me}, 7.78; 6,8-\text{Me}, 8.58 \text{d}(J 6.7); \] 
\[ 8.88 \text{d}(J 5.3); \text{aliphatic H(6)}, 7.0-9.0 \text{m} \alpha \] 
6.15, 6.15, 6.27

(129) 60  
\[ 3,5'-\text{H}, 2.53; \text{ca. 2.73} \alpha \] 
4-Me, 7.78; 6,8-Me, 8.68d(J 6.4); 
8.91d(J 5.0); aliphatic H(6), 6.9-9.0m; 4'-OMe, 6.44

(130) 60  
\[ \text{ArH}(3), 2.55-2.8 \text{m}, \text{ca. 3.06} \text{br}; \] 
\[ \text{Ar-Me}, 7.43, 7.43, 7.59; \] 
aliphatic H, 5.86d(J 5.2); 
6.2-7.7m(3); NH, 6.2-7.7?

(135) 100  
\[ \text{ArH}(4), 5'-\text{H}, 2.2-2.53 \text{m}; \] 
4-H, 1.71d; J3,4 8.6; 
8-Me, 7.17

(136) 60  
\[ \text{ArH}(4), 5'-\text{H}, 2.3-2.7 \text{m}; 4-\text{H}, 1.90d; J3,4 8.0; 8-\text{Me}, 7.30; \] 
4'-OMe, 6.67

(144) 100  
\[ 1-\text{Me}, 7.38; \text{ArH}(3), 2.8-2.95 \text{m}; \] 
5-H, 3.08d; 6-H, 2.07d; 
J5,6 10.0; -CH2.CHE-, see Table 8.

(145) 100  
\[ 2,4-\text{H}, 3.08, 3.15; 5-\text{H}, 3.17d; 6-\text{H}, 2.14d; \] 
J5,6 9.4; Ar-Me, 7.45, 7.71; 
-CH2.CHE-, 5.68t, 6.92q, 
ca. 7.7m; J's ca. 10-13

(146) 60  
\[ 2,4-\text{H}, 3.02 \text{br}; 6-\text{H}, 2.29; \text{ca. 7.7m} \alpha \] 
6.13, 6.30, 6.33

photo-isomer of (146) 60  
\[ \text{ArH}(3), 2.4-2.8 \text{m} \alpha \] 
Ar-Me, 7.38, 7.56, 7.65 
aliphatic H(3), 6.5-7.8m \alpha 
6.08, 6.32, 6.36, 6.36, 6.50, 7.11
Numbers of protons, where necessary, are given in parentheses. Ar = aromatic, br = broad, d = doublet, m = multiplet, q = quartet, t = triplet.

\[ ^{a} \text{Partly obscured by other resonances.} \quad ^{b} \text{Centre of six-line multiplet.} \quad ^{c} \text{Apparent singlet.} \quad ^{d} \text{Broad, indicating further coupling.} \quad ^{e} \text{Measured by J.K.Stubbs.} \quad ^{f} \text{These assignments could be reversed.} \quad ^{g} \text{8 lines.} \quad ^{h} \text{Ethyl ester.} \quad ^{i} \text{7 lines.} \quad ^{j} \text{Non-equivalent methyl groups.} \quad ^{k} \text{Completely obscured by other resonances.} \quad ^{l} \text{See Table 3.} \quad ^{m} \text{Obtained from spectrum of red-adduct mixture; other resonances not distinguishable from those of first red adduct (89a).} \quad ^{n} \text{Shows splitting of ca. 0.9Hz.} \quad ^{o} \text{No change on shaking with D}_2\text{O.} \]
| TABLE 11 |
| Mass Spectra |

\( m/e \), with % of base peak in parentheses; \( m^* \) = metastable-ion peak, \( br \) = broad.

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<tr>
<th>(28)²⁶</th>
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<tbody>
<tr>
<td>427 ( (M^+, 18.0) ), 412 ( (9.0) ), 396 ( (6.0) ), 368 ( (7.0) ),</td>
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<tr>
<td>342 ( (21.0) ), 341 ( (100.0) ), 336 ( (14.0) ), 310 ( (25.0) ),</td>
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<tr>
<td>283 ( (8.0) ), 252 ( (9.0) ), 241 ( (6.0) ), 238 ( (10.5) ), 208 ( (5.0) ),</td>
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<tr>
<td>191 ( (8.0) ), 149 ( (11.0) ) (other peaks &lt;5%)</td>
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<tr>
<td>441 ( (M^+, 48) ), 410 ( (21) ), 382 ( (20) ), 355 ( (100) ), 350 ( (100) ),</td>
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<tr>
<td>323 ( (100) ), 290 ( (15) ), 265 ( (55) ), 237 ( (26) ), 207 ( (76) ),</td>
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<tr>
<td>204 ( (32) ), 179 ( (16) ) (other peaks &lt;15%), ( m^* 294 )</td>
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<tr>
<td>( (323+308) ), 286 ( (441+355) ), 217.5 ( (323+265) ), 161.5</td>
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<td>( (265+207) )</td>
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<tr>
<td>503 ( (M^+, 10) ) 417 ( (100) ), 412 ( (17) ), 282 ( (11) ), 265 ( (12) ),</td>
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<td>240 ( (13) ) (other peaks &lt;10%), ( m^* 346 ) ( (503+417) )</td>
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<td>457 ( (M^+, 17) ), 426 ( (5) ), 398 ( (7) ), 371 ( (100) ), 366 ( (5) ),</td>
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<td>356 ( (5) ), 340 ( (12) ), 338 ( (1) ), 313 ( (1) ), 282 ( (5) ),</td>
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<td>268 ( (8) ), ( m^* 336.5 ) ( (398+366) ), 311.5 ( (371+340) ),</td>
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<td>( (301.5 ), ( (457+371) )</td>
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<td>441 ( (M^+, 20) ), 410 ( (13) ), 382 ( (8) ), 355 ( (100) ), 350 ( (14) ),</td>
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<tr>
<td>323 ( (56) ), 265 ( (13) ), 207 ( (20) ), 204 ( (11) ) (other peaks &lt;10%), ( m^* 294 ) ( (323+308) ), 286 ( (441+355) )</td>
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<tr>
<td>441 ( (M^+, 16) ), 410 ( (4) ), 382 ( (4) ), 355 ( (4) ), 350 ( (7) ),</td>
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<td>341 ( (100) ), 322 ( (7) ), 310 ( (48) ), 290 ( (6) ), 283 ( (6) ),</td>
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<td>252 ( (18) ), 238 ( (26) ), 204 ( (12) ), 193 ( (8) ), ( m^* 356 )</td>
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<tr>
<td>( (410+382) ), 321 ( (382+350) ), 282 ( (341+310) ), 263.8</td>
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<tr>
<td>( (441+341) ), 166 ( (310+238) )</td>
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<td>497 ( (M^+, 10) ), 452 ( (4) ), 424 ( (4) ), 383 ( (100) ), 378 ( (15) ),</td>
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<tr>
<td>350 ( (6) ), 338 ( (7) ), 311 ( (28) ), 276 ( (7) ), 266 ( (32) ),</td>
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<tr>
<td>264 ( (12) ), 239 ( (12) ), 238 ( (15) ), 220 ( (18) ), 205 ( (7) ),</td>
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<tr>
<td>194 ( (8) ), 193 ( (8) ) (other peaks &lt;4%), ( m^* 337 ) ( (424+378) ),</td>
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<tr>
<td>295 ( (497+383) ), 252.5 ( (383+311) )</td>
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<tr>
<td>503 ( (M^+, 0.04) ), 471 ( (1.5) ), 412 ( (0.8) ), 384 ( (100) ),</td>
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<tr>
<td>310 ( (5) ), 282 ( (2) ), 252 ( (7) ), 238 ( (7) ) (other peaks &lt;2%), ( m^* 282 ) ( (341+310) )</td>
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</table>
(71) 441 (M+, 7), 410 (2), 382 (0.5), 341 (100), 322 (2), 310 (19), 252 (7), 238 (9), 204 (2), 193 (2), m* 282 (341→310), 263.8 (441+341), 166 (310+238)

(88a) 569 (M+, 4), 539 (2), 510 (3), 478 (1), 450 (2), 425 (100), 394 (2), 366 (16), 334 (12), 322 (8), 308 (7), 276 (6), 218 (4), 217 (4), 204 (6), 191 (7), 190 (8), 128 (4), 114 (5), 113 (30), 85 (16), 59 (26), m* 457 (569+510), 315.5 (425+366), 304.5 (366+334)

(89a) 583 (M+, 7.5), 568 (21), 552 (6), 524 (7), 439 (100), 408 (9), 380 (15), 376 (8.5), 364 (3.5), 348 (65), 320 (24), 316 (22.5), 302 (5), 288 (12), 258 (8), 202 (14), 114 (17.5), 113 (100), 101 (2.5), 85 (25), 59 (15) (other peaks <6%), m* 483 (568+524), 328 (439+380), 319 (380+348)

(90a) 597 (M+, 2), 582 (9), 566 (1), 538 (6), 453 (100), 446 (1), 422 (8), 405 (1), 394 (19), 390 (5), 388 (3), 378 (3), 366 (10), 362 (71), 334 (21), 330 (23), 316 (7), 304 (9), 302 (11), 272 (21), 260 (10), 218 (17), 217 (24), 216 (45), 215 (19), 205 (10), 204 (10), 202 (21), 192 (10), 113 (42), 85 (40), 59 (39) (other peaks <10%), m* 497 (582+538), 342 (453+394)

(90b) 597 (M+, 7.2), 582 (17.6), 566 (4.0), 538 (11.4), 506 (1.2), 478 (1.8), 464 (1.8), 453 (100), 446 (1.2), 422 (5.8), 405 (1.6), 394 (8.6), 378 (3.8), 362 (40.4), 346 (1.6), 334 (10.4), 330 (11.2), 302 (4.2), 272 (4.4), 216 (6.8), 113 (32.2), 85 (3.2), 59 (6.8) (other peaks <6%), m* 567 (597+582), 497 (582+438), 393 (453+422), 342 (453+394), 301 (362+330)

(96) 505 (M+, 100), 503 (M+, 100), 474 (2.5), 472 (2.5), 446 (18), 444 (16), 414 (11), 412 (10), 402 (1.5), 400 (1.5), 388 (6), 386 (5), 356 (5), 354 (4), 270 (2.5), 256 (2.5), 254 (10), 223 (4), 222 (4), 189 (4), 188 (7) (other peaks <4%), m* 393br (505→446, 503→444), 383br (446→414, 444→412)
(97) 425 (M+, 100), 394 (4.5), 366 (15), 334 (10),
322 (2), 308 (5), 276 (4.5), 204 (4), 191 (5),
190 (5.5), 183 (9.5), m* 315.5 (425+366), 304.8
(366+334)

(100) 467 (M+, 0.2), 439 (100), 408 (5), 407 (9), 380 (29),
375 (6), 364 (19), 348 (39), 336 (2), 321 (9),
320 (11), 310 (15), 262 (9), 232 (6), 218 (9),
204 (24), 203 (11), 128 (11), 59 (26) (other
peaks <10%), m* 377.5 (439+407), 345.4 (407+375),
329 (439+380), 319 (380+348), 297, 270.5

(104) 575 (M+, 56), 544 (4), 543 (2), 516 (49), 502 (1),
484 (13), 456 (8), 431 (11), 430 (7), 424 (4),
399 (10), 398 (6), 340 (8), 339 (9), 338 (12),
312 (12), 310 (8), 302 (26), 286 (100), 280 (20),
278 (12), 274 (10), 259 (10), 254 (63), 242 (16),
241 (10), 196 (12), 168 (11), 167 (10), 131 (20),
130 (18), 113 (18), 105 (23), 91 (11), 85 (5),
59 (27), 55 (21) (other peaks <15%), m* 514 (575+544),
463 (575+516), 454 (516+484), 323 (575+431), 225.5
(286+254)

(105) 589 (M+, 34), 558 (11), 531 (231), 530 (75), 498 (6),
470 (7), 445 (40), 444 (15), 413 (12), 412 (9),
354 (22), 353 (10), 352 (17), 326 (48), 325 (22),
300 (86), 294 (39), 268 (59), 182 (13), 144 (18),
113 (28), 91 (8), 85 (10), 59 (100) (other peaks
<10%), m* 477 (489+530), 468 (530+498), 336 (589+
445), 239.4 (300+268), 383.3 (445+413), 265.5 (326+
294)

(106) 573 (M+, 35), 542 (1), 541 (1), 515 (9), 514 (35),
500 (6), 482 (9), 454 (13), 444 (1), 429 (28),
422 (19), 397 (25), 369 (93), 365 (9), 362 (4),
338 (67), 337 (99), 310 (10), 284 (28), 278 (25),
252 (18), 220 (10), 218 (10), 193 (11), 192 (10),
192 (10), 113 (58), 85 (12), 59 (100) (other peaks
<10%), m* 461.8 (573+514), 511br (573+542, 541),
452 (514+482), 392.2 (454+422), 367.4 (429+397),
343.0 (397+369), 307.7 (369+337), 229.3 (337+278)
(110) 725 (M+, 4), 694 (5), 693 (4), 666 (5), 634 (4), 606 (6), 581 (79), 574 (1), 551 (1), 550 (1), 524 (2), 523 (2), 522 (2), 490 (3), 478 (2), 462 (7), 439 (19), 430 (4), 404 (2), 403 (2), 380 (2), 374 (2), 372 (2), 228 (3), 227 (3), 144 (3), 113 (100), 85 (53), 82 (6), 81 (3), 59 (39) (other peaks <3%), m* 663 br (725+694, 693), 640 (694+666), 612.5 (725+666), 603.6 (666+634), 579.3 (634+606)

(124) 579 (M+, 69), 564 (100), 549 (28), 548 (89), 547 (77), 534 (12), 532 (18), 520 (90), 506 (10), 490 (11), 488 (16), 474 (11), 462 (13), 461 (20), 460 (25), 430 (8), 406 (12), 405 (16); 404 (13), 403 (18), 402 (14), 346 (16), 285 (11), 258 (17), 242 (15), (other peaks <11%), m* 467 (579+520)

(126) 581 (M+, 66), 550 (25), 536 (2), 522 (100), 508 (2), 490 (27), 446 (26), 438 (21), 437 (78), 422 (9), 421 (7), 406 (68), 405 (43), 404 (22), 389 (20), 376 (14), 346 (20), 302 (10), 260 (10), 259 (12), 232 (12), 231 (11), 113 (62), 105 (12), 91 (19), 85 (36), 77 (17), 59 (47), 55 (28) (other peaks <12%), m* 469 (581+522), 460 (522+490), 328.7 (581+437)

(127) 437 (M+, 100), 422 (7), 406 (29), 405 (27), 390 (2), 378 (2), 346 (2), 289 (3), 261 (3), 260 (3), 233 (4), 232 (6), 231 (5), 230 (4), 203 (3), 59 (7), m* 375.5 (437+405), 327 (437+378)

(130) 441 (M+, 32), 410 (11), 383 (54), 382 (100), 354 (3), 327 (6), 322 (21), 290 (3), 269 (4), 264 (59), 236 (10), 209 (4), 208 (4), 196 (9), 170 (7), 59 (11), m* 331 (441+382), 271.5 (382+322)

(135) 409 (M+, 100), 394 (6), 378 (37), 377 (35), 362 (1), 350 (1), 349 (1), 346 (1.5), 261 (1), 233 (1), 204 (10), 202 (11), 191 (5), 189 (4) (other peaks <1%), m* 348 br (409+378, 377), 317 br (378, 377+346)

(144) 583 (M+, 30.5), 552 (11.5), 524 (100), 492 (21.5), 464 (9), 460 (16.5), 448 (4), 432 (8), 406 (10),
141

374 (13), 292 (5.5), 228 (81), 215 (17.5), 142 (8.5),
m* 498 (552+524), 471 (583+524), 462 (524+492),
430.2 (492+460), 405br (460+432), 228 (374+292?),
89.2 (583+228)

(145)

597 (M+, 16), 566 (6), 538 (40), 506 (9), 474 (7),
446 (1), 420 (1), 388 (3), 242 (100), 229 (14),
59 (8), m* 511.4 (566+538), 485 (597+538), 476
(538+506), 440 (506+474), 420 (474+446), 98.1
(597+242)

(146)

611 (M+, 12), 580 (3), 552 (39), 520 (5), 488 (1),
460 (1), 434 (1), 402 (7), 320 (1), 256 (100),
243 (30), 211 (6), 170 (10), 168 (8), m* 498.6
(611+552), 490 (552+520), 458 (520+488), 372.5
(434+402), 322, 183, 107.3 (611+256)

photo-
isomer of
(146)

611 (M+, 100), 580 (8), 553 (10), 552 (33), 508 (92),
493 (14), 492 (15), 476 (2), 461 (4), 446 (17),
434 (13), 402 (29), 401 (11), 374 (12), 370 (13),
343 (11), 342 (13), 330 (7), 257 (14), 256 (12),
101 (9), 77 (11), (other peaks <7%), m* 550 (611+580),
499 (611+552)

—a Measured by J.K.Stubbs. — b Spectrum of pyrolysis
— product almost identical. — c Spectrum of Gagan's tetra-
hydro-derivative°,71 almost identical.
PART TWO

Chapter 5

The "Blue" Adducts from Substituted 2-Methylquinolines and Dimethyl Acetylenedicarboxylate
Gagan isolated deep blue adducts in low yield from the reactions of 2-methyl-\(^5\) and 2,8-dimethyl-quinoline\(^6\) with dimethyl acetylenedicarboxylate. On the basis of the analytical data and the n.m.r. spectra he assigned molecular weights of 679 and 693 to these adducts respectively, corresponding to a composition of 1 mole quinoline + 4 moles ester - 1 mole methanol. Certain differences in the n.m.r. spectra (discussed below) led him to believe that these adducts were not simple analogues.

Caterer obtained the mass spectra, and on the basis of the u.v., n.m.r. and mass spectral data he assigned structures.\(^7\) He considered that the two adducts were analogues, although he was unable to explain the differences in the n.m.r. spectra on this basis. Neither Gagan nor Caterer offered any chemical evidence regarding the structures of these compounds.

In the present investigation deep blue adducts have been isolated in extremely low yield from the reactions of 2,6,8-trimethylquinoline and 2-ethylquinoline with dimethyl acetylenedicarboxylate; the i.r., u.v., n.m.r. and mass spectra suggest that these compounds are closely related to the above two blue adducts.

Two experiments with the blue adduct from 2-methylquinoline have already been described in the Experimental Section of Part 1 (p. 120). Treatment of this adduct with bromine in glacial acetic acid gave in low yield a dark green, isomeric compound. An attempted reduction with zinc in glacial
acetic acid gave only unstable polymeric ester. Gagan attempted to hydrogenate this adduct in the presence of 10% palladium-on-charcoal but obtained a material which was rapidly oxidised in air during extraction from the reaction mixture.

It thus appeared unlikely that it would be possible to elucidate the structures of these blue adducts by chemical means, since: (i) the adducts are formed in very low yield, and it is thus extremely difficult to obtain quantities (1-2g.) adequate for a study of their chemical reactions. On one occasion Gagan obtained 3.7g. blue adduct from 20g. 2-methylquinoline, but from 10g. 2,8-dimethylquinoline he obtained only 0.3g. blue adduct. In the present investigation, the blue adducts from 2,6,8-trimethylquinoline and 2-ethylquinoline were isolated in only milligram amounts. (ii) the information obtained from the reactions of the 2-methylquinoline adduct discussed above is very limited. The fact that an isomer is formed on treatment of the 2-methylquinoline adduct with bromine in glacial acetic acid suggests the possibility of geometric isomerism (cf. the first and second red adducts) as well as of structural isomerism, but in the absence of further information this is of little assistance in the assignment of a structure.

Accordingly a determination of the structure of the 2-methylquinoline blue adduct by means of X-ray crystallography was attempted, under the supervision of Dr. C.K. Prout. The structures of several acetylenic-ester adducts have been solved by this method recently. Very regrettably this
attempt failed, for reasons which are discussed along
with the experimental details at the end of this chapter.
It has therefore not been possible to elucidate the structures
of the blue adducts during the present investigation.

The spectral data of the blue adducts will now be
discussed. Caterer's mass spectrum of the 2-methylquinoline
blue adduct shows a small peak at $m/e$ 693 (679 + 14), but
in a repeat spectrum a peak at this mass number was scarcely
discernible. The molecular weight obtained from the X-ray
study is 679, confirming Gagan's$^{5,70}$ original assignment,
and so this peak appears to be spurious. Caterer's mass
spectrum of the 2,8-dimethylquinoline blue adduct shows a
small peak at $m/e$ 707, again fourteen mass numbers higher
than expected for Gagan's molecular weight of 693. However
a repeat spectrum run using a carefully purified sample of
the adduct also showed this feature, and in view also of
certain differences in the n.m.r. spectra (discussed below)
of these two adducts, it is conceivable that the molecular
weight of the 2,8-dimethylquinoline blue adduct is 707.
This would correspond to a composition of 1 mole quinoline
+ 4 moles ester - 1 mole water, giving a structure involving
one additional carbon atom and two additional hydrogen atoms.
The integration of the n.m.r. spectrum (ester region) is
insufficiently accurate to exclude the presence of two extra
protons; elemental analysis likewise is insufficiently accurate
to distinguish between these alternatives.

The n.m.r. spectrum of the 2-methylquinoline blue adduct
in deuteriochloroform solution (Table 12, p. 152 ) shows
the presence of six aromatic protons, two of which appear as doublets at 1.84 and 2.79\(\tau\) \((J 9.0 \text{ Hz})\); the spectrum in trifluoroacetic acid solution shows one-proton doublets at 0.73 and ca. 1.9\(\tau\) \((J 7.2 \text{ Hz})\). These two protons thus appear to be the 3- and 4-protons of the parent quinoline, the doublets at 1.84 \((\text{CDCl}_3)\) and 0.73\(\tau\) \((\text{TFA})\) being assigned to the 4-proton. The partial structures (151) and (153) are thus suggested. The spectrum of the 2,8-dimethylquinoline adduct \((\text{Table 12})\) shows the presence of five aromatic protons; however the low-field doublet at 1.93\(\tau\) \((J 9.2 \text{ Hz})\) shows further splitting of 1.5 Hz, and instead of a high-field doublet there is a one-proton doublet of doublets centred at 2.99\(\tau\) \((J 9.1, 6.3 \text{ Hz})\). The corresponding partial structures (152) and (154) do not explain this pattern, and for this reason Gagan\(^7^0\) believed that these adducts were not analogues; Caterer\(^7^1\) was unable to explain these differences. The partial structure (155) is a possible alternative.\(^7^0\)
The spectra of the 2-methyl- and 2,8-dimethyl-quinoline adducts show one-proton doublets at 4.90 (J 7.0) and 5.29 (J 4.9) respectively. Integration shows that in each case coupling is to a proton whose resonances are obscured by ester-methyl resonances, suggesting the presence of a -CH-E-CHE- grouping as in the red adducts. The spectrum of the 2-methylquinoline adduct also shows a high-field ester-methyl resonance.

The mass spectrum of the 2-methylquinoline adduct shows a strong peak at m/e M-144, and that of the 2,8-methylquinoline adduct shows a strong peak at m/e 549 (693-144); the peaks of the spectrum of dimethyl fumarate are also present, as with the red adducts. This provides further evidence in favour of a -CH-E-CHE- grouping, and indicates that the elements of dimethyl fumarate (maleate) are eliminated in the mass spectrometer.

The n.m.r. spectrum of the 2,6,8-trimethylquinoline blue adduct (Table 12) suggests that this adduct is an analogue of the 2,8-dimethylquinoline blue adduct. The mass spectrum indicates that the molecular weight is 721, fourteen greater than the new, alternative molecular weight of the 2,8-dimethylquinoline adduct (707). The n.m.r.
The u.v. spectra of the blue adducts (Table 13) are very similar and show extremely broad absorptions in the visible region, centred at 600-620 nm. Caterer suggested that these broad bands are charge-transfer bands; in support of this suggestion, he observed that the wavelength of this absorption is solvent-dependent. The maximum for the 2-methylquinoline adduct occurs at 646 nm in chloroform, 626 nm in dimethyl sulphoxide and 616 nm in methanol; the polarity of the solvent is expected to influence charge-separation.

The blue adducts are protonated in strongly-acid solution, giving yellow colours. Addition of a few drops of 2N caustic soda to methanolic solutions of the blue adducts also gives a yellow colour, an observation which escaped both Gagan and Caterer.

The isomer of the 2-methylquinoline blue adduct obtained by treatment with bromine in glacial acetic acid is a very deep green in colour. The n.m.r. spectrum is very similar to that of the parent blue adduct, except that the resonances of the six aromatic protons form a single multiplet in the range 2.1-3.2τ, with no obvious low- or
high-field doublets. The mass spectrum indicates a molecular weight of 679 but shows only a very small peak at m/e M-144. Addition of 2N caustic soda to a methanolic solution does not discharge the green colour completely, and a yellow colour is obtained in only extremely strong acid (ca. 9:1 72% HClO₄: MeOH).

The structures suggested by Caterer⁷¹ for the 2-methyl- and 2,8-dimethyl-quinoline blue adducts are (156) and (157) respectively. Structure (156) is not incompatible with the observed spectra, but structure (157) is open to objections on the grounds of the n.m.r. and possibly the mass spectra, as discussed above. Charge-transfer is permitted, as shown;

\[
\begin{align*}
(156) \\
(157) \text{i-Me}
\end{align*}
\]

indeed, Caterer pointed out that the comparatively low \(\tau\)-values of the 5- and 6-protons of this structure (cf. those of the corresponding protons in the red adducts) indicate a fairly large initial positive charge on the
nitrogen atom. However it is again emphasised that Caterer's structures were proposed solely on spectral grounds, without any supporting chemical evidence.

Other highly-coloured acetylenic ester adducts have been reported. The highly-conjugated cyclopenta[cd] cycl-[3,3,3]azine (158) and related compounds prepared by Leaver et al.\textsuperscript{116} are green; the u.v. spectra show complex bands in the region 500-700 nm. The blue pyridinium salts of the anions (159) and (160) are formed by treatment of dimethyl acetylenedicarboxylate with malononitrile and ethyl cyanoacetate respectively in the presence of pyridine and acetic acid.\textsuperscript{117}

\[
\begin{align*}
\text{(158)} \\
(159) \ R = \text{CN} \\
(160) \ R = \text{CO}_2\text{Et}
\end{align*}
\]
The u.v. spectra of these resonance-stabilised anions show absorptions at 668 nm (159) and 625 nm (160). The corresponding acids, obtained by protonation of the anions in solution, are colourless and appear to be dimeric in structure.\textsuperscript{117,118}
Table 12

N.m.r. Spectra of the Blue Adducts
(60 MHz, CDCl₃ solution; t-values, J in Hz)

<table>
<thead>
<tr>
<th>Blue Adduct from</th>
<th>Proton Assignments</th>
<th>Ester-CH₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Me-quinoline</td>
<td>ArH, 1.84d (1), 2.79d (1), J 9.0, 6.10, 6.17— and 2.0-2.7m (4); 4.90d (1), J 7.0, and 6.0-6.5 (1) ²</td>
<td>6.26 (12), 6.28, 6.73</td>
</tr>
<tr>
<td>do. b, c</td>
<td>ArH, 0.73 (1), ca. 1.9 (1); J 7.2, 5.7-6.3 (18), and 1.5-1.9m (4); 4.72br (1); 5.7-6.3 (1) ³</td>
<td>6.68</td>
</tr>
<tr>
<td>2-Me-quinoline, isomer</td>
<td>ArH (6), 2.1-3.2m; 5.05d (1), J 7.1, and 6.1-6.4 (1) ²</td>
<td>6.21, 6.21, 6.21, 6.33</td>
</tr>
<tr>
<td>2,8-Me₂-quinoline</td>
<td>ArH: 1.93 (1), J 9.2; 2.2-2.6m (3); 2.99 (1), d of d (J 9.1, 6.3), 5.29d (1), J 4.9 and 6.0-6.55 (1); Ar-Me, 7.51</td>
<td>6.1-6.5m (21)</td>
</tr>
<tr>
<td>2,6,8-Me₃-quinoline</td>
<td>ArH: 2.15d (1), J 8.6; 2.5-2.8m (2); 3.20t (1), J 8.0; 5.38d (1), J 5.3, and 6.0-6.6 (1); Ar-Me, 7.59, 7.59</td>
<td>6.0-6.6m (21)</td>
</tr>
<tr>
<td>2-Et-quinoline</td>
<td>ArH (6), 1.9-2.9m; 5.0d (1), J 7.2; 6.0-6.5 (4?) ³</td>
<td>6.0-6.4m (18), 6.80</td>
</tr>
</tbody>
</table>

² Obscured by ester-methyl resonances. ³ In trifluoroacetic acid. ⁴ At 100 MHz. ⁵ Peaks show further splitting of 1.5 Hz. ⁶ 4 lines. ⁷ Shows signs of further splitting.
<table>
<thead>
<tr>
<th>Blue Adduct from</th>
<th>Solvent*</th>
<th>$\lambda_{\text{max.}}$ (nm) ($10^{-4} \epsilon$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Me-quinoline</td>
<td>M</td>
<td>246 (2.31), 283 (1.60), 294 (1.54),</td>
</tr>
<tr>
<td></td>
<td></td>
<td>330 (2.96), 616very br (2.50)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>272 (3.26), 354 (1.47), 398 (1.03)</td>
</tr>
<tr>
<td></td>
<td>MB</td>
<td>235 (3.72), 318infl.(0.94), 387 (1.25)</td>
</tr>
<tr>
<td>2-Me-quinoline, isomer</td>
<td>M</td>
<td>247 (2.14), 286 (1.45), 342 (3.18),</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>635very br (2.19)</td>
</tr>
<tr>
<td></td>
<td>MB</td>
<td>237 (3.42), 283infl.(1.44), 348 (1.17),</td>
</tr>
<tr>
<td></td>
<td></td>
<td>406 (1.46), 629very br (0.43)</td>
</tr>
<tr>
<td>2,8-Me$_2$-a quinoline</td>
<td>M</td>
<td>253 (1.58), 302 (1.32), 336 (2.12),</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>609very br (1.55)</td>
</tr>
<tr>
<td></td>
<td>MB</td>
<td>241 (2.54), 266infl. (2.08), 394 (1.04)</td>
</tr>
<tr>
<td>2,6,8-Me$_3$-b quinoline</td>
<td>M</td>
<td>254 (1.75), 303 (1.46), 335 (1.69),</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>599very br (1.35)</td>
</tr>
<tr>
<td></td>
<td>MB</td>
<td>240 (2.60), 260infl.(2.26), 307 (1.02)</td>
</tr>
<tr>
<td>2-Et-quinoline</td>
<td>M</td>
<td>244 (2.48), 284 (1.70), 294 (1.62),</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>330 (2.98), 615very br (2.44)</td>
</tr>
<tr>
<td></td>
<td>MB</td>
<td>232br (4.03), 318 (1.02), 385 (1.34)</td>
</tr>
</tbody>
</table>

*Solvents: M, MB, P as before; A = MeOH:HC10$_4$ 1:9.

a Calculated for M.W. = 693.  b M.W. 721.
<table>
<thead>
<tr>
<th>Blue Adduct</th>
<th>m/e (% base peak)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blue Adduct from</strong></td>
<td></td>
</tr>
<tr>
<td>2-Me-\textsuperscript{71}quinoline</td>
<td>679 (M\textsuperscript{+}, 26.8), 648 (17.0), 621 (12.0), 620 (31.5), 588 (13.0), 535 (100), 508 (24.0), 507 (77.0), 476 (17.5), 449 (35.0), 448 (9.0), 418 (8.5), 404 (8.8), 391 (8.0), 333 (14.4), 238 (12.0), 113 (24.0), 85 (8.2), 59 (9.3) (other peaks &lt;8%), m* 566 (679→620), 480.5 (535→507), 421.6 (679→535), 397.4 (507→449)</td>
</tr>
<tr>
<td>2-Me-quinoline, isomer</td>
<td>679 (M\textsuperscript{+}, 0.05), 665 (0.1), 651 (2), 620 \textsuperscript{{20}}, 592 (2), 507 (24), 479 (4), 476 (3), 448 (3), 217 (0.9), 144 (4), 113 (100), 85 (17), 59 (10), m* 452.5 (507→479), 395.5 (651→507), 64 (113→85)</td>
</tr>
<tr>
<td>2,8-Me\textsubscript{2}-quinoline</td>
<td>707 (0.1), 693 (M\textsuperscript{+}, 32), 678 (3), 662 (25), 650 (19), 635 (12), 634 (38), 618 (2), 606 (46), 602 (8), 574 (7), 549 (17), 521 (100), 490 (9), 486 (7), 463 (5), 458 (19), 228 (5), 142 (12), 113 (26), 85 (3), 59 (35), m* 580 (693→634), 565 (650→606), 495br (549→521)</td>
</tr>
<tr>
<td>2,6,8-Me\textsubscript{3}-quinoline</td>
<td>721 (M\textsuperscript{+}, 30), 708 (20), 707 (59), 691 (21), 676 (20), 660 (13), 649 (17), 648 (37), 632 (100), 616 (19), 588 (10), 535 (18), 113 (50), 85 (28), 59 (100), m* 594 (707→648), 578 (691→632)</td>
</tr>
<tr>
<td>2-Et-quinoline</td>
<td>693 (M\textsuperscript{+}, 0.1), 679 (0.8), 620 (0.5), 604 (0.5), 592 (0.3), 588 (0.3), 574 (0.2), 551 (1), 535 (3), 519 (1), 507 (1.5), 492 (1), 46 (2.5), 446 (1), 227 (8), 181 (3), 144 (3), 113 (100), 100 (3), 85 (49), 82 (7), 59 (70), 54 (32), 53 (36) (other peaks &lt;6%)</td>
</tr>
</tbody>
</table>
Attempted Determination of the Structure of the 2-Methylquinoline Blue Adduct by X-Ray Crystallography.

Crystal data: crystals from slowly evaporating methanol-acetonitrile are orthorhombic, \( \mathbf{a} = 22.084, \quad \mathbf{b} = 18.059, \quad \mathbf{c} = 16.027 \text{ Å}; \quad \alpha = \beta = \gamma = 90^\circ; \quad \mathbf{U} = 6391.81 \text{ Å}^3; \quad \mathbf{D}_m = 1.420 \pm 0.004 \) (by flotation in petrol/ carbon tetrachloride), \( \mathbf{D}_c \) for 8 \( \mathbf{C}_{33} \mathbf{H}_{29} \mathbf{N}_1 \mathbf{O}_{15} \) = 1.41, and for 8 \( \mathbf{C}_{34} \mathbf{H}_{31} \mathbf{N}_1 \mathbf{O}_{15} \) = 1.44 g cm\(^{-3}\). Space group \( \mathbf{P} \mathbf{b} \mathbf{c} \mathbf{a} \); Cu- \( \mathbf{K}_\alpha \) radiation, \( \lambda = 1.5418 \text{ Å} \).

3,225 independent reflections were recorded by the equi-inclination, multiple-film Weissenberg technique up to and including the 13th layer. The intensities were estimated visually and corrected for Lorentz and polarisation effects but not absorption. Reflections on different film packs were scaled on the basis of exposure times.

After obtaining an overall scale factor and a temperature factor from a Wilson plot,\(^{119} \) normalised structure factors (E)\(^{119} \) were calculated (Table 15) and used in the Centro-symmetric Symbolic Addition Programme of O.J.R. Hodder.\(^{120} \) Three origin reflections were chosen, but the total atomic contents of the unit cell were so great that no solution could be determined with a reasonable probability criterion. The signs of ca. 200 reflections were determined for one solution with five symbols, a significance limit\(^{120} \) of 1.0 and \( \mathbf{E}_s \not\geq 1.5 \), but none of the resultant E- maps gave any chemically reasonable information.

Cause of failure: the most likely cause of the failure is thought to be that the atomic contents of the unit cell
(392 non-hydrogen atoms) were too great for the C.S.S.A. programme to handle, as stated above. It is known that the limit for this programme occurs in the region of 400 atoms.

However, a zero-layer photograph taken towards the end of the investigation showed a number of significant differences from one taken ca. five months previously. This may indicate that the crystal underwent chemical change over the period of six months during which it was mounted on the camera. Incorrect indexing is not thought to be a cause of failure, as no mistakes have so far been found despite careful checking.

Preliminary photographs were also taken of a crystal of the 2,8-dimethylquinoline blue adduct; these showed that the crystal was triclinic. Accordingly, no further attention was given to this compound, as the visual interpretation and indexing of photographs of a triclinic crystal, compared with those of an orthorhombic crystal, is exceptionally difficult.
Table 15

Normalised Structure Factors

<table>
<thead>
<tr>
<th>*</th>
<th>k</th>
<th>l</th>
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<tbody>
<tr>
<td></td>
<td>$h_1$</td>
<td>$E_1$</td>
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<tr>
<td></td>
<td>$h_2$</td>
<td>$E_2$</td>
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**Note:** The table above contains a sequence of numbers arranged in a grid format. Each row and column is labeled with a number, and the intersections of these numbers represent the values in the grid. The exact nature of the sequence is not clear from the image.
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REFERENCES
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64 R. Huisgen and K. Herbig, Annalen, 1965, 688, 98; R. Huisgen, M. Morikawa, K. Herbig and E. Brunn,

74 ibid., p. 201.
77 Mrs. R.F. Flowerday, private communication.
82 ibid., p.206.
94 L.M. Jackman and S. Sternhell, op.cit. (ref. 73),p.270.
98 O. Doebner, Annalen, 1887, 242, 272.
99 O. Doebner, ibid., p.270.
100 A. Combes, Compt. Rend., 1887, 106, 143.
108 O. Doebner, Annalen, 1887, 242, 279.
109 cf. ref. 96.
110 cf. ref. 78.
111 ref. 103, op.cit., p.1473.


120 C.S.S.A. Programme, Department of Chemical Crystallography, University of Oxford.
ABSTRACT
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This thesis is divided into two parts. The first part concerns the chemistry of products obtained from substituted 2-methylquinolines and dimethyl acetylenedicarboxylate, and the second part describes an attempted X-ray crystallographic structure determination of one of these products, the structure of which could not be elucidated by chemical methods.

In Part 1, Chapter 1, the previously known types of reactions of nitrogen-containing heterocycles with acetylenecarboxylic acids and their esters are reviewed. The investigations reported here concern new reactions between substituted 2-methylquinolines and dimethyl acetylenedicarboxylate; also, some previously described reactions were reinvestigated. These reactions usually gave complex mixtures which were resolved chromatographically. A number of separate types of product were formed, and these types are considered in separate chapters.

In Chapter 2 the benzo[c]quinolizines and azepines such as (1) and (2), and the isomeric azepine (3), obtained from the reactions of substituted 2-methylquinolines with dimethyl acetylenedicarboxylate are discussed.

(1)  (2)  (3)
Scheme 1
The u.v., n.m.r., i.r. and mass spectra of these compounds are entirely analogous to those of known benzo[c]quinolizines and azepines.\textsuperscript{1} New azepines (4), (5) and (6) were obtained from 2-ethylquinoline and (7)\textsuperscript{2} from 2-benzylquinoline; their structures were deduced from the u.v., n.m.r. and mass spectra.

\begin{align*}
(4) & \\
(5) E = \text{CO}_2\text{Et} &
\end{align*}

The isolation of these compounds with a methyl- or a phenyl-group at position 10 or 11 has necessitated a re-appraisal of one mechanism of azepine-formation,\textsuperscript{1} and a new scheme involving a spiro intermediate is proposed (Scheme 1).

The 4a-isopropyl-4aH-benzo[c]quinolizine (8) is the sole product of the reaction of 2-isopropylquinoline with dimethyl acetylenedicarboxylate; this undergoes a smooth photo-isomerisation to the 1-isopropyl-1H-benzo[c]quinolizine (9).
Chapter 3 discusses the "red" adducts formed in the reactions of 2-methyl-, 2,8-dimethyl- and 2,6,8-trimethylquinoline with dimethyl acetylenedicarboxylate. Two red adducts are formed in each of these reactions, and it is proposed that these are geometric isomers of the structures (10), (11) and (12) respectively.

The n.m.r. spectra of these compounds show the 6- and 7-protons as AX quartets in the range 2.8-3.5\(\tau\); the 11- and 12-protons and the 17-protons appear as AX quartets and singlets respectively in the range 4.4-6.2\(\tau\). The chemical shifts of the 11-, 12- and 17-protons permit a simple classification into two groups, "first" and "second" red adducts. Shielding of the 11-ester methyl groups of the
first red adducts, but not of their isomers, by the benzo-
ring causes these methyl resonances to occur upfield from
the other ester-methyl resonances. The n.m.r. spectra in
trifluoroacetic acid solution are discussed. The red adducts
readily eliminate the elements of dimethyl fumarate (maleate)
in the mass spectrometer.

The first red adducts from 2-methyl- and 2,8-dimethyl-
quinoline are most conveniently prepared pure by using
methanol as the reaction solvent, as the first red, but not
the second red, adducts crystallise from the reaction mixture.
Bromination of the first red adduct from 2-methylquinoline
gives the quinoline (13), which is readily debrominated to

give the quinoline (14). Compound (14) is also obtained
directly by treatment of the first red adduct from 2-methyl-
quinoline with zinc in glacial acetic acid. Formation of
compounds (13) and (14) involves the elimination of fumarate
(maleate) from the red-adduct molecules, as also occurs in
the mass spectrometer. This facile elimination, when
considered in conjunction with the shielding effects observed
in the n.m.r. spectra, provides good evidence in favour of a red-adduct structure involving a saturated-CHE.CHE-grouping attached to the nitrogen atom.

Hydrogenation of the first red adducts from 2-methyl- and 2,8-dimethyl-quinoline in glacial acetic acid solution using Adams' catalyst gives the hexahydro-derivatives (15) and (16) respectively; the tetrahydro-derivative (17) is obtained from the 2-methylquinoline adduct using 10% palladium-on-charcoal. The spectral properties of the derivatives (13) - (17) are discussed.

![Chemical structures](image)

A mechanism to account for the formation of the red adducts is proposed. Alternative structures for the red adducts, and the reasons for rejecting them, are discussed. The surprising observation that the benzo[c]quinolizines, azepines¹ and other adducts (Chapter 4) formed when these 2-methylquinolines are reacted with dimethyl acetylene-dicarboxylate in acetonitrile solution, are not formed when methanol is used as the reaction solvent, is noted.
A red compound isolated in very low yield from the reaction of 2,4-dimethylquinoline with dimethyl acetylene-dicarboxylate in methanol is assigned the structure (18) on spectral evidence.

Chapter Four deals with other adducts isolated from the reactions of substituted 2-methylquinolines with dimethyl acetylene-dicarboxylate. Analogues of the known adduct (19) are obtained from 2,8-dimethyl-, 2,6,8-trimethyl- and 2,4,6,8-tetramethyl-quinoline (compounds (20)-(22) respectively).

An adduct assigned the structure (23) on the basis of the n.m.r. and u.v. spectra is obtained in very low yield from 2,4,6,8-tetramethylquinoline.

The adduct (24) is also obtained from 2,4,6,8-tetramethylquinoline, although the alternative structure (25), and
corresponding structures for the degradation products, are not excluded. Catalytic reduction of this adduct using Adams' catalyst gives the phenols (26) and (27) by hydrogenolysis; the ether (28) is readily formed from the phenol (27) by methylation with ethereal diazomethane. Mixtures obtained by treating adduct (24) with both bromine and zinc in glacial acetic acid are discussed. Mechanisms accounting for the formation of both structures (24) and (25) are presented; it is not possible to differentiate between these structures on the basis of the present work.

Yellow adducts isolated from the reactions of 2,8-di- methyl-, 2,6,8-trimethyl- and 2,4,6,8-tetramethylquinoline with dimethyl acetylenedicarboxylate are tentatively assigned the structures (29) - (31) respectively. A computer-simulated
n.m.r. spectrum is in good agreement with the observed AMX pattern of the \(-\text{CH}_2-\text{CHE}-\) grouping of adduct (29) in the range 5.4-7.9\(\pi\). Irradiation of a methanolic solution of the adduct (31) with ultra-violet light yields a photo-isomer.

Part 2, Chapter 5, concerns the "blue" adducts formed in the reactions of 2-methyl-, 2,8-dimethyl-, 2,6,8-trimethyl- and 2-ethyl-quinoline with dimethyl acetylene-dicarboxylate, the latter two of which were first isolated in the present investigation. The 2-methylquinoline blue adduct has a molecular weight of 679, corresponding to a composition of 1 mole quinoline + 4 moles ester - 1 mole methanol. Treatment of this adduct with bromine in glacial acetic acid yields a dark green isomer, but an attempted reduction with zinc in glacial acetic acid gave only polymeric ester. As the information obtainable from these reactions, and from the spectral data of the blue adducts, was very
limited, an attempt was made to determine the structure of the 2-methylquinoline blue adduct by X-ray crystallography. This attempt failed, the most likely reason being that the total atomic contents of the unit cell were too great for the available computer programme to handle.

The n.m.r., u.v. and mass spectra of the blue adducts are discussed. The n.m.r. spectra suggest that the 2-methyl- and 2,8-dimethyl-quinoline adducts may not be analogues; the mass spectrum of the latter suggests that the molecular weight could be 707, and not 693 as stated by Gagan. The extremely broad absorption bands in the visible spectra of the adducts appear to be charge-transfer bands.

References
2 isolated by J.K. Stubbs.
3 cf. ref 1.
6 Centrosymmetric Symbolic Addition Programme, Department of Chemical Crystallography, University of Oxford.